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The application was originally filed in English.

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NOVEL USE

Field of the Invention

This invention relates to the use of imidazopyridine derivatives as inhibitors of the kinase Itk. Certain novel imidazopyridine derivatives are also disclosed together with processes for their preparation, pharmaceutical compositions comprising them, and their use in therapy.

Background of the Invention

Inducible T cell Kinase (Itk) is a member of the Tec-family of cytosolic protein tyrosine kinases. In mammalians, this family also includes Btk, Tec, Bmx, and Txk. These kinases regulate various immune cell functions that integrate signals given by the other cytosolic tyrosine kinases as well as serine/threonine kinases, lipid kinases, and small G proteins. Tec-family kinases have the following general structure: a N-terminal pleckstrin-homology (PH) domain, a Tec-homology domain that includes a Btk motif and one or two proline-rich (PR) motifs, a SH3 domain, a SH2 domain and a c-terminal catalytic (SH1) domain. These kinases are expressed exclusively in hematopoietic tissues, with the exception of Tec and Bmx that have also been detected in endothelial cells. The cellular distribution is different for the Tec-family members. For example, Itk is expressed by T cells, NK cells and mast cells, whereas Btk is expressed by all hematopoietic cells except T cells. Thus, hematopoietic cells may express one or several Tec-family kinases. For example, T cells express Itk, Tec and Txk, and mast cells express Btk, Itk and Tec.

Btk is by far the most extensively studied among the Tec-family kinases, due to its association with X-linked agammaglobulinemia (XLA), and Btk is currently the only Tec-family kinase with a known human phenotype. XLA patients are virtually devoid of mature B cells and their Ig levels are strongly reduced.

$Itk^{-/-}$ mice show defects in T cell activation and differentiation. T helper 2 (Th2) differentiation is disrupted in these mice, whereas Th1 differentiation is apparently intact.

In T and B cells, signalling through T cell receptors and B cell receptors leads to activation of Itk and Btk, respectively. Downstream of Itk and Btk a number of different messengers are engaged; scaffolding proteins (SLP-76, LAT, SLP-65), Src kinases, MAP kinases, and PI3-K. These events are followed by PLC-γ activation that leads to IP3 generation and sustained Ca^{2+} flux, and subsequently activation of transcription factors. PLC-γ1 has been suggested as a direct substrate for Itk.

In T cells, Itk (and Tec) may also mediate signalling through the CD28 co-receptor. Furthermore, Itk has in T cells been implicated in the activation of β-integrin.

Signalling from Tec-family kinases can also be regulated by PH domain-mediated plasma membrane localization, and by Src-family-mediated phosphorylation of critical tyrosine residues. Interestingly, Itk, Btk and Txk have recently been shown to translocate to the nucleus after activation.

From studies using Itk-/- mice, it has been proposed that Itk is required for Th2 but not Th1 cell development. This was demonstrated in the *N. brasiliensis* and *L. major* infection models where the Itk-/- animals are protected in the Leishmania model indicating an intact Th1 response, whereas they are susceptible to infection with *N. Brasiliensis* that requires an intact Th2 response for resolution of the infection. This indicates that modulation of Itk activity may prove useful for treatment of Th2-driven disorders and conditions.

We have identified the critical role of Itk in regulating important mast cell and basophil functions and established that the activity of mast cells or basophils may be inhibited through inhibition of Itk. Thus Itk inhibitors may be used as pharmaceutical agents for the treatment of mast cell-driven or basophil-driven conditions or diseases. In particular, we have identified Itk as a target for inhibiting several key events in both acute and late phase allergic reactions common to allergic rhinitis and asthma.

EP 209 707 discloses particular fused imidazo derivatives, including some imidazopyridines, and their use as potential cardiovascular agents.

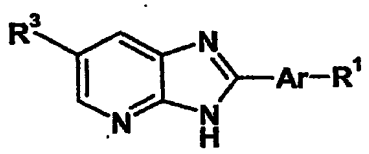
DE 2 305 339 and US 3,985,891 disclose certain imidazopyridine derivatives potentially useful as cardiotonics, anticoagulants and as agents for altering blood pressure.

None of the above publications are concerned with compounds that have utility as inhibitors of the kinase Itk.

The present invention discloses 2-aryl-substituted derivatives of 6-substituted-3H-imidazo[4,5-b]pyridines that are useful as Itk inhibitors.

Disclosure of the Invention

The present invention provides the use of a compound of formula (I)



(I)

wherein:

R^3 represents halogen, C1 to 3 alkyl or C1 to 3 alkoxy;

Ar represents phenyl, a 5- or 6-membered heteroaromatic ring or an indole ring; said heteroaromatic ring incorporating 1 to 3 heteroatoms independently selected from O, N and S; said phenyl, heteroaromatic or indole ring being optionally further substituted by chloro or OMe;

R^1 represents H, halogen, CN, C1 to 6 alkyl, NO_2, SO_2Me, C1 to 6 alkynyl, CH_2OH, phenyl, OR^2 or $(CH_2)_nNR^4R^5$;

n represents an integer 0 or 1;

R^2 represents H or C1 to 4 alkyl; said C1 to 4 alkyl being optionally further substituted by a group selected from Ar^1, $CONH_2$, CO_2Et, OH, NR^6R^7, halogen and epoxy; and when substituted by NR^6R^7 or halogen, said alkyl is optionally further substituted by OH;

R^4 represents H or C1 to 4 alkyl;

R^5 represents H, C1 to 6 alkyl, C2 to 6 alkanoyl or CH_2Ar^2;

or the group $-NR^4R^5$ together represents a 5 to 7 membered saturated azacyclic ring optionally incorporating one additional heteroatom selected from O, S and NR^8;

R^6 represents H, C1 to 4 alkyl or $CH_2CH_2OCH_3$;

R^7 represents H, C1 to 6 alkyl, C3 to 6 cycloalkyl, Ar^3, a 5 or 6 membered saturated or partially unsaturated heterocyclic ring incorporating 1 or 2 heteroatoms selected independently from O, N and S and optionally substituted by Me, Et or CO_2Et; said C1 to 6 alkyl being optionally substituted by one or more groups selected independently from OH, CN, $CONMe_2$, CONHMe, C1 to 4 alkoxy, halogen, NMe_2, Ar^4, and a 5 or 6 membered saturated heterocyclic ring incorporating 1 or 2 heteroatoms selected independently from O, N and S and optionally also incorporating a carbonyl group; said C3 to 6 cycloalkyl being optionally substituted by OH or CN;

or the group $-NR^6R^7$ together represents a 5 to 7 membered saturated azacyclic ring optionally incorporating 1 additional heteroatom selected from O and NR^9; and optionally

substituted by one or more substituents selected independently from OH, NMe_2, $CONH_2$, CH_2OH, CH_2CH_2OH, phenyl, pyridyl, piperidinyl or methoxyphenyl;

R^8 represents H, C1 to 6 alkyl or CH_2Ph;

R^9 represents CH_2CH_2OH, $COCH_3$, Me, CO_2Et, CH_2CH_2OMe or a six membered aromatic or azaaromatic ring optionally further substituted by one or more substituents selected independently from Cl, CN, OMe and CF_3;

Ar^1 represents phenyl, thiazolyl or thiadiazolyl, optionally further substituted by halogen;

Ar^2 represents phenyl, a 5- or 6-membered heteroaromatic ring or a benzimidazole ring; said heteroaromatic ring incorporating 1 to 3 heteroatoms independently selected from O, N and S; said phenyl or heteroaromatic or benzimidazole ring being optionally further substituted by one or two groups independently selected from halogen, C1 to 4 alkyl, CN, CH_2OH, C1 to 4 alkoxy, CO_2Me, CH_2OAc and pyridyl;.

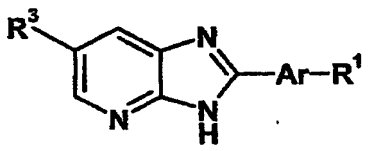
Ar^3 represents thiazolyl, triazolyl or tetrazolyl;

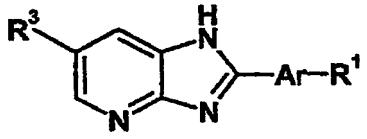
Ar^4 represents phenyl, a 5- or 6-membered heteroaromatic ring or an indole ring; said heteroaromatic ring incorporating 1 to 3 heteroatoms independently selected from O, N and S; said phenyl, heteroaromatic or indole ring being optionally further substituted by one or two groups independently selected from halogen and OMe;

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of diseases or conditions in which inhibition of kinase Itk activity is beneficial.

The compounds of formula (I) may exist in enantiomeric forms. All enantiomers, diastereoisomers, racemates and mixtures thereof are included within the scope of the invention.

It will be readily apparent to the man skilled in the art that compounds of general formula (I) may exist in tautomeric forms as illustrated below:





All such tautomeric forms and mixtures thereof are included within the scope of the present invention.

In one embodiment, R^3 in formula (I) represents halogen. In another embodiment, R^3 in formula (I) represents bromo.

In another embodiment, Ar in formula (I) represents phenyl optionally further substituted by chloro or methoxy.

In another embodiment, R^1 in formula (I) represents OR^2 or $(CH_2)_nNR^4R^5$.

In another embodiment, R^2 in formula (I) represents $CH_2CHOHCH_2NR^6R^7$.

In another embodiment, R^2 in formula (I) represents $CH_2CH_2NR^6R^7$.

In another embodiment, R^1 in formula (I) represents $NR^4CH_2Ar^2$.

In one aspect, the invention provides the use of a compound of formula (I) wherein

R^3 represents halogen; Ar represents phenyl optionally further substituted by chloro or OMe; R^1 represents OR^2 or $(CH_2)_nNR^4R^5$; R^2 represents C2 to 4 alkyl; said C2 to 4 alkyl being optionally further substituted by NR^6R^7 or by both OH and NR^6R^7; and NR^4R^5 represents $NR^4CH_2Ar^2$; or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of diseases or conditions in which inhibition of the kinase Itk activity is beneficial.

Unless otherwise indicated, the term "C1 to 6 alkyl" referred to herein denotes a straight or branched chain alkyl group having from 1 to 6 carbon atoms. Examples of such groups include methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, t-butyl, pentyl and hexyl. The terms C1 to 4 alkyl, C1 to 3 alkyl and C2 to 4 alkyl are to be interpreted analogously.

Unless otherwise indicated, the term "C1 to 6 alkynyl" referred to herein denotes a straight or branched chain alkyl group having from 1 to 6 carbon atoms and including at least one carbon-carbon triple bond. Examples of such groups include ethynyl, propynyl and butynyl.

Unless otherwise indicated, the term "C3 to 6 cycloalkyl" referred to herein denotes a saturated carbocyclic ring having from 3 to 6 carbon atoms. Examples of such groups include cyclopropyl, cyclopentyl and cyclohexyl.

Unless otherwise indicated, the term "C2 to 6 alkanoyl" referred to herein denotes a straight or branched chain alkyl group having from 1 to 5 carbon atoms bonded to the remainder of the molecule via a carbonyl group. Examples of such groups include acetyl, propionyl and butyryl.

Unless otherwise indicated, the term "C1 to 4 alkoxy" referred to herein denotes an oxygen substituent bonded to a straight or branched chain alkyl group having from 1 to 4 carbon atoms. Examples of such groups include methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy,

i-butoxy and s-butoxy. The term "C1 to 3 alkoxy" referred to herein is to be interpreted analogously.

Unless otherwise indicated, the term "halogen" referred to herein denotes fluorine, chlorine, bromine and iodine.

Examples of a 5- or 6-membered heteroaromatic ring incorporating 1 to 3 heteroatoms independently selected from O, N and S, include pyridyl, thienyl, furyl, pyrrolyl, imidazolyl, triazolyl, thiadiazolyl, pyrazolyl, pyrazinyl, thiazolyl and isoxazolyl.

Examples of a 5 to 7 membered saturated azacyclic ring optionally incorporating one additional heteroatom selected from O, S and N include pyrrolidine, piperidine, piperazine, morpholine and thiomorpholine.

Examples of a 5 or 6 membered saturated or partially unsaturated heterocyclic ring incorporating 1 or 2 heteroatoms selected independently from O, S and N include tetrahydrofuran, tetrahydropyran, pyrrolidine, pyrroline, piperidine, piperazine and morpholine.

Examples of a 5 or 6 membered saturated heterocyclic ring incorporating 1 or 2 heteroatoms selected independently from O, S and N and optionally also incorporating a carbonyl group include tetrahydrofuran, tetrahydropyran, tetrahydropyranone, pyrrolidine, pyrrolidinone, piperidine, piperidinone, piperazine and morpholine.

Examples of a 6 membered aromatic or azaaromatic ring include phenyl, pyridyl, pyrazinyl and pyrimidinyl.

The use of the following compounds of formula (I) and pharmaceutically acceptable salts thereof is specifically included within the present invention:

4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenol

N-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]propyl}-*N*,*N*-dimethylamine

6-bromo-2-{4-[(5-chloro-1,2,3-thiadiazol-4-yl)methoxy]phenyl}-3*H*-imidazo[4,5-*b*]pyridine

6-bromo-2-{4-[(2-chloro-1,3-thiazol-5-yl)methoxy]phenyl}-3*H*-imidazo[4,5-*b*]pyridine

6-bromo-2-[4-(2-{4-[3-chloro-5-(trifluoromethyl)pyridin-2-yl]piperazin-1-yl}ethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine

6-bromo-2-[4-(2-piperidin-1-ylethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine

[5-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)-2-furyl]methanol

6-bromo-2-(7-methyl-1H-indol-3-yl)-3H-imidazo[4,5-b]pyridine

6-bromo-2-(1-phenyl-1H-1,2,3-triazol-4-yl)-3H-imidazo[4,5-b]pyridine

6-bromo-2-(1H-pyrrol-2-yl)-3H-imidazo[4,5-b]pyridine

6-bromo-2-(1H-pyrazol-3-yl)-3H-imidazo[4,5-b]pyridine

6-bromo-2-(4-bromo-1H-pyrazol-3-yl)-3H-imidazo[4,5-b]pyridine

6-bromo-2-(2-methyl-1H-imidazol-5-yl)-3H-imidazo[4,5-b]pyridine

4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)-2-methoxyphenol

4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)-2-chlorophenol

4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)-3-methoxyphenol

4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)-3-chlorophenol

N-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)-3-methoxyphenyl]-N,N-dimethylamine

2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethanol

6-bromo-2-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridine

6-bromo-2-(2-methylphenyl)-3H-imidazo[4,5-b]pyridine

6-bromo-2-(2-methoxyphenyl)-3H-imidazo[4,5-b]pyridine

6-bromo-2-(4-isopropoxyphenyl)-3H-imidazo[4,5-b]pyridine

4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)benzonitrile

2-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenol

6-bromo-2-(4-isopropylphenyl)-3H-imidazo[4,5-b]pyridine

6-bromo-2-(4-methoxyphenyl)-3H-imidazo[4,5-b]pyridine

6-bromo-2-(3-methoxyphenyl)-3H-imidazo[4,5-b]pyridine

2-[4-(benzyloxy)-3-methoxyphenyl]-6-bromo-3H-imidazo[4,5-b]pyridine

6-bromo-2-thien-3-yl-3H-imidazo[4,5-b]pyridine

6-bromo-2-(4-tert-butylphenyl)-1H-imidazo[4,5-b]pyridine

N-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenyl]-N,N-dimethylamine

6-bromo-2-(4-pyrrolidin-1-ylphenyl)-3H-imidazo[4,5-b]pyridine

6-bromo-2-[4-(methylsulfonyl)phenyl]-3H-imidazo[4,5-b]pyridine

N,N-dimethyl-N-[4-(6-methyl-3H-imidazo[4,5-b]pyridin-2-yl)phenyl]amine

2-(4-isopropoxyphenyl)-6-methyl-3H-imidazo[4,5-b]pyridine

6-bromo-2-(4-nitrophenyl)-3H-imidazo[4,5-b]pyridine

N-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenyl]acetamide

2-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]acetamide

ethyl [4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]acetate

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-methylamine

6-bromo-2-[4-(3-chloropropoxy)phenyl]-3H-imidazo[4,5-b]pyridine

3-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]propan-1-amine

6-bromo-2-[4-(3-morpholin-4-ylpropoxy)phenyl]-3H-imidazo[4,5-b]pyridine

6-bromo-2-[4-(3-piperidin-1-ylpropoxy)phenyl]-3H-imidazo[4,5-b]pyridine

6-bromo-2-[4-(3-pyrrolidin-1-ylpropoxy)phenyl]-3H-imidazo[4,5-b]pyridine

6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine

6-bromo-2-[4-(2-morpholin-4-ylethoxy)phenyl]-3H-imidazo[4,5-b]pyridine

N-{2-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]ethyl}-*N*-(tetrahydrofuran-2-ylmethyl)amine

6-bromo-2-[4-(2-pyrrolidin-1-ylethoxy)phenyl]-3H-imidazo[4,5-b]pyridine

2-[{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}(methyl)amino]ethanol

3-[{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}(methyl)amino]propanenitrile

6-bromo-2-[4-(2-morpholin-4-ylethoxy)phenyl]-3H-imidazo[4,5-b]pyridine

1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}pyrrolidin-3-ol

6-bromo-2-{4-[2-(4-methylpiperazin-1-yl)ethoxy]phenyl}-3H-imidazo[4,5-b]pyridine

1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N,N-dimethylpyrrolidin-3-amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N,1-dimethylpyrrolidin-3-amine

N^2-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N^1,N^1,N^2-trimethylglycinamide

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-ethyl-N',N'-dimethylethane-1,2-diamine

N-benzyl-N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-methylamine

2-{4-[2-(4-acetylpiperazin-1-yl)ethoxy]phenyl}-6-bromo-3H-imidazo[4,5-b]pyridine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N,N-bis(2-methoxyethyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-methyl-N-(2-phenylethyl)amine

6-bromo-2-{4-[2-(4-phenylpiperazin-1-yl)ethoxy]phenyl}-3H-imidazo[4,5-b]pyridine

6-bromo-2-{4-[2-(4-pyridin-2-ylpiperazin-1-yl)ethoxy]phenyl}-3H-imidazo[4,5-b]pyridine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-[3-(1H-imidazol-1-yl)propyl]amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(4-methoxybenzyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(3-methoxybenzyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(4-chlorobenzyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(3-chlorobenzyl)amine

ethyl 4-({2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}amino)piperidine-1-carboxylate

6-bromo-2-(4-{2-[4-(2-methoxyethyl)piperazin-1-yl]ethoxy}phenyl)-3H-imidazo[4,5-b]pyridine

1-({2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}amino)propan-2-ol

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(2-methoxyethyl)amine

2-({2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}amino)propan-1-ol

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(2-furylmethyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(tetrahydrofuran-2-ylmethyl)amine

N-benzyl-N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(pyridin-3-ylmethyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(pyridin-4-ylmethyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(thien-2-ylmethyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(1-phenylethyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-1-ethylpiperidin-3-amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(2-morpholin-4-ylethyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(2-methoxybenzyl)amine

1-[3-({2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}amino)propyl]pyrrolidin-2-one

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-[2-(4-chlorophenyl)ethyl]amine

4-[{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}(methyl)amino]cyclohexanecarbonitrile

1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperidin-3-ol

6-bromo-2-{4-[2-(2-pyridin-3-ylpiperidin-1-yl)ethoxy]phenyl}-3H-imidazo[4,5-b]pyridine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-cyclopentylamine

1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-4-phenylpiperidin-4-ol

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-[2-(1H-imidazol-4-yl)ethyl]amine

1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperidine-3-carboxamide

6-bromo-2-{4-[2-(4-pyrazin-2-ylpiperazin-1-yl)ethoxy]phenyl}-3H-imidazo[4,5-b]pyridine

(1*S*,2*S*)-2-({2-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]ethyl}amino)cyclohexanol

6-bromo-2-(4-{2-[4-(3-methoxyphenyl)piperazin-1-yl]ethoxy}phenyl)-3H-imidazo[4,5-b]pyridine

(1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperidin-4-yl)methanol

4-({2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}amino)cyclohexanol

(1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperidin-2-yl)methanol

1'-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-1,4'-bipiperidine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-1,3-thiazol-2-amine

1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperidine-4-carboxamide

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-1H-1,2,4-triazol-3-amine

2-(4-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperazin-1-yl)benzonitrile

6-(4-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperazin-1-yl)nicotinonitrile

1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}prolinamide

6-bromo-2-(4-{2-[4-(2-methoxyphenyl)piperidin-1-yl]ethoxy}phenyl)-3H-imidazo[4,5-b]pyridine

2-(4-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperazin-1-yl)ethanol

1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperidin-4-ol

6-bromo-2-(4-{2-[4-(2-methoxyphenyl)piperazin-1-yl]ethoxy}phenyl)-3H-imidazo[4,5-b]pyridine

(2*S*)-2-({2-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]ethyl}amino)-3-methylbutan-1-ol

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-4,5-dihydro-1,3-thiazol-2-amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-[2-(1H-indol-3-yl)ethyl]amine

(2*S*)-2-({2-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]ethyl}amino)-2-phenylethanol

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-1H-tetrazol-5-amine

(1*S*,2*R*)-2-({2-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]ethyl}amino)cyclohexanol

6-methoxy-2-(4-methoxyphenyl)-3H-imidazo[4,5-b]pyridine

6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-pyrrolidin-1-ylpropan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-morpholin-4-ylpropan-2-ol

1-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}pyrrolidin-3-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-piperidin-1-ylpropan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-(diethylamino)propan-2-ol

1-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}piperidin-4-ol

1-(4-acetylpiperazin-1-yl)-3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[3-(dimethylamino)pyrrolidin-1-yl]propan-2-ol

4-[({2-hydroxy-3-[4-(6-methyl-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]propyl}amino)methyl]phenol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(2-hydroxyethyl)(methyl)amino]propan-2-ol

3-[{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}(methyl)amino]propanenitrile

4-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}piperazin-1-ol

N^2-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}-N^1,N^1,N^2-trimethylglycinamide

1-[benzyl(methyl)amino]-3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[methyl(2-phenylethyl)amino]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-(4-phenylpiperazin-1-yl)propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-(4-pyridin-2-ylpiperazin-1-yl)propan-2-ol

1-[2-({3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}amino)ethyl]imidazolidin-2-one

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(3-methoxybenzyl)amino]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(2-chlorobenzyl)amino]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(4-chlorobenzyl)amino]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(3-chlorobenzyl)amino]propan-2-ol

ethyl 4-({3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}amino)piperidine-1-carboxylate

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[4-(2-methoxyethyl)piperazin-1-yl]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-(cyclopropylamino)propan-2-ol

3-({3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}amino)propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(2-methoxyethyl)amino]propan-2-ol

2-({3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}amino)propan-1-ol

1-(benzylamino)-3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(pyridin-3-ylmethyl)amino]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(pyridin-4-ylmethyl)amino]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(1-ethylpiperidin-3-yl)amino]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(2-morpholin-4-ylethyl)amino]propan-2-ol

1-[3-({3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}amino)propyl]pyrrolidin-2-one

1-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}piperidin-3-ol

1-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}prolinamide

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[4-(hydroxymethyl)piperidin-1-yl]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[2-(hydroxymethyl)piperidin-1-yl]propan-2-ol

1-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}piperidine-4-carboxamide

1-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}piperidine-3-carboxamide

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[4-(2-hydroxyethyl)piperazin-1-yl]propan-2-ol

2-(4-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}piperazin-1-yl)benzonitrile

6-(4-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}piperazin-1-yl)nicotinonitrile

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-chloropropan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-(1,3-thiazol-2-ylamino)propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-(4-pyrazin-2-ylpiperazin-1-yl)propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(2-methoxybenzyl)amino]propan-2-ol

4-[{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}(methyl)amino]cyclohexanecarbonitrile

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-(2-pyridin-3-ylpiperidin-1-yl)propan-2-ol

1-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}-4-phenylpiperidin-4-ol

2-({3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}amino)-3-methylbutan-1-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[4-(3-methoxyphenyl)piperazin-1-yl]propan-2-ol

4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline

4-({[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]amino}methyl)benzonitrile

N-benzyl-N-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenyl]amine

N-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenyl]-N-(1H-imidazol-2-ylmethyl)amine

N-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenyl]-N-(1H-imidazol-5-ylmethyl)amine

3-({[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenyl]amino}methyl)benzonitrile

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(4-methoxybenzyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(2-methoxybenzyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(3-methoxybenzyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(2-chlorobenzyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(4-chlorobenzyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(1*H*-pyrazol-3-ylmethyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(3-chlorobenzyl)amine

[5-({[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]amino}methyl)-2-furyl]methanol

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(thien-2-ylmethyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(2-furylmethyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(thien-3-ylmethyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(4-methyl-1*H*-imidazol-5-yl)methyl]amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(3-furylmethyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(1,3-thiazol-2-ylmethyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(4-bromothien-2-yl)methyl]amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(1*H*-imidazol-4-ylmethyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(2-methyl-1*H*-imidazol-5-yl)methyl]amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(3,5-dimethylisoxazol-4-yl)methyl]amine

[5-({[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]amino}methyl)-2-furyl]methyl acetate

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(5-pyridin-2-ylthien-2-yl)methyl]amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(1-methyl-1*H*-benzimidazol-2-yl)methyl]amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(2-ethyl-1*H*-imidazol-5-yl)methyl]amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(1-methyl-1*H*-imidazol-5-yl)methyl]amine

methyl 4-({[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]amino}methyl)-1-methyl-1*H*-pyrrole-2-carboxylate

6-bromo-2-[4-(morpholin-4-ylmethyl)phenyl]-3*H*-imidazo[4,5-*b*]pyridine

N-benzyl-5-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)pyridin-2-amine

5-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)-*N*-(3-methoxybenzyl)pyridin-2-amine

6-bromo-2-(6-morpholin-4-ylpyridin-3-yl)-3*H*-imidazo[4,5-*b*]pyridine.

A more particular aspect of the invention provides the use of a compound of formula (I), or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of allergic, autoimmune, inflammatory, proliferative and hyperproliferative diseases and immune-mediated diseases including rejection of transplanted organs or tissues and Acquired Immunodeficiency Syndrome (AIDS).

According to the invention there is also provided a method of treating, or reducing the risk of, diseases or conditions in which inhibition of kinase Itk activity is beneficial, which comprises administering to a person suffering from or at risk of said disease or condition, a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt thereof.

More particularly, there is also provided a method of treating, or reducing the risk of allergic, autoimmune, inflammatory, proliferative and hyperproliferative diseases and immune-mediated diseases including rejection of transplanted organs or tissues and Acquired Immunodeficiency Syndrome (AIDS), which comprises administering to a person suffering from or at risk of said disease or condition, a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt thereof.

Examples of these conditions are:

(1) **(the respiratory tract)** airways diseases including chronic obstructive pulmonary disease (COPD) such as irreversible COPD; asthma, such as bronchial, allergic, intrinsic, extrinsic and dust asthma, particularly chronic or inveterate asthma (for example, late asthma and airways hyper-responsiveness); bronchitis; acute, allergic, atrophic rhinitis and chronic rhinitis including rhinitis caseosa, hypertrophic rhinitis, rhinitis purulenta, rhinitis sicca and rhinitis medicamentosa; membranous rhinitis including croupous, fibrinous and pseudomembranous rhinitis and scrofoulous rhinitis; seasonal rhinitis including rhinitis nervosa (hay fever) and vasomotor rhinitis; sarcoidosis, farmer's lung and related diseases, fibroid lung and idiopathic interstitial pneumonia; sinusitis, chronic rhinosinusitis, nasosinusal polyposis; pulmonary fibrosis;

(2) **(bone and joints)** rheumatoid arthritis, seronegative spondyloarthropathies (including ankylosing spondylitis, psoriatic arthritis and Reiter's disease), Behcet's disease, Sjogren's syndrome and systemic sclerosis;

(3) **(skin)** psoriasis, atopical dermatitis, contact dermatitis and other eczmatous dermitides, seborrhoetic dermatitis, Lichen planus, Pemphigus, bullous Pemphigus, Epidermolysis bullosa, urticaria, angiodermas, vasculitides, erythemas, cutaneous eosinophilias, uveitis, Alopecia areata and vernal conjunctivitis;

(4) **(gastrointestinal tract)** Coeliac disease, proctitis, eosinopilic gastro-enteritis, mastocytosis, Crohn's disease, ulcerative colitis, food-related allergies which have effects remote from the gut, for example, migraine, rhinitis and eczema;

(5) **(other tissues and systemic disease)** multiple sclerosis, atherosclerosis, Acquired Immunodeficiency Syndrome (AIDS), lupus erythematosus, systemic lupus, erythematosus, Hashimoto's thyroiditis, myasthenia gravis, type I diabetes, nephrotic syndrome, eosinophilia fascitis, hyper IgE syndrome, lepromatous leprosy, sezary syndrome and idiopathic thrombocytopenia pupura; tuberculosis;

(6) **(allograft rejection)** acute and chronic following, for example, transplantation of kidney, heart, liver, lung, bone marrow, skin and cornea; and chronic graft versus host disease.

We are particularly interested in Th2-driven and/or mast cell-driven and/or basophil-driven conditions or diseases.

Thus, a more particular aspect of the invention provides the use of a compound of formula (I) or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of Th2-driven and/or mast cell-driven and/or basophil driven diseases or conditions; and a method of treating, or reducing the risk of, Th2-driven and/or mast cell-driven and/or basophil driven diseases or conditions which comprises administering to a person suffering from or at risk of, said disease or condition, a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt thereof.

In a preferred aspect of the invention, we provide a method for the treatment or prevention of a reversible obstructive airway disease, especially asthma, which comprises administering a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt thereof to a human that is suffering from or susceptible to the disease. We also provide the use of a compound of formula (I) or a pharmaceutically

acceptable salt thereof in the manufacture of a medicament for the treatment or prevention of a reversible obstructive airway disease, especially asthma.

In another preferred aspect of the invention, we provide a method for the treatment or prevention of rhinitis which comprises administering a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt thereof to a human that is suffering from or susceptible to rhinitis, especially allergic rhinitis. We also provide the use of a compound of formula (I) or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment or prevention of rhinitis, especially allergic rhinitis.

Prophylaxis is expected to be particularly relevant to the treatment of persons who have suffered a previous episode of, or are otherwise considered to be at increased risk of, the disease or condition in question. Persons at risk of developing a particular disease or condition generally include those having a family history of the disease or condition, or those who have been identified by genetic testing or screening to be particularly susceptible to developing the disease or condition.

For the above mentioned therapeutic indications, the dose of the compound to be administered will depend on the compound employed, the disease being treated, the mode of administration, the age, weight and sex of the patient. Such factors may be determined by the attending physician. However, in general, satisfactory results are obtained when the compounds are administered to a human at a daily dosage of between 0.1 mg/kg to 100 mg/kg (measured as the active ingredient).

The compounds of formula (I) may be used on their own, or in the form of appropriate pharmaceutical formulations comprising the compound of the invention in combination with a pharmaceutically acceptable diluent, adjuvant or carrier. Particularly preferred are compositions not containing material capable of causing an adverse reaction, for example, an allergic reaction. Conventional procedures for the selection and preparation of suitable

pharmaceutical formulations are described in, for example, "Pharmaceuticals - The Science of Dosage Form Designs", M. E. Aulton, Churchill Livingstone, 1988.

In another aspect the invention provides a pharmaceutical formulation comprising a therapeutically effective amount of a compound of formula (I), or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier, for use in the treatment or prophylaxis of diseases or conditions in which inhibition of kinase Itk activity is beneficial.

In a more particular aspect, the invention provides a pharmaceutical formulation comprising a therapeutically effective amount of a compound of formula (I), or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier, for use in the treatment or prophylaxis of allergic, autoimmune, inflammatory, proliferative and hyperproliferative diseases and immune-mediated diseases including rejection of transplanted organs or tissues and Acquired Immunodeficiency Syndrome (AIDS).

According to the invention, there is provided a pharmaceutical formulation comprising preferably less than 95% by weight and more preferably less than 50% by weight of a compound of formula (I) in admixture with a pharmaceutically acceptable diluent or carrier.

We also provide a method of preparation of such pharmaceutical formulations that comprises mixing the ingredients.

The compounds may be administered topically, for example, to the lungs and/or the airways, in the form of solutions, suspensions, HFA aerosols or dry powder formulations, for example, formulations in the inhaler device known as the Turbuhaler® ; or systemically, for example, by oral administration in the form of tablets, pills, capsules, syrups, powders or granules; or by parenteral administration, for example, in the form of sterile parenteral

solutions or suspensions; or by rectal administration, for example, in the form of suppositories.

Dry powder formulations and pressurized HFA aerosols of the compounds of the invention may be administered by oral or nasal inhalation. For inhalation, the compound is desirably finely divided. The finely divided compound preferably has a mass median diameter of less than 10 μm, and may be suspended in a propellant mixture with the assistance of a dispersant, such as a C_8-C_{20} fatty acid or salt thereof, (for example, oleic acid), a bile salt, a phospholipid, an alkyl saccharide, a perfluorinated or polyethoxylated surfactant, or other pharmaceutically acceptable dispersant.

The compounds of the invention may also be administered by means of a dry powder inhaler. The inhaler may be a single or a multi dose inhaler, and may be a breath actuated dry powder inhaler.

One possibility is to mix the finely divided compound with a carrier substance, for example, a mono-, di- or polysaccharide, a sugar alcohol, or an other polyol. Suitable carriers are sugars, for example, lactose, glucose, raffinose, melezitose, lactitol, maltitol, trehalose, sucrose, mannitol; and starch. Alternatively the finely divided compound may be coated by another substance. The powder mixture may also be dispensed into hard gelatine capsules, each containing the desired dose of the active compound.

Another possibility is to process the finely divided powder into spheres which break up during the inhalation procedure. This spheronized powder may be filled into the drug reservoir of a multidose inhaler, for example, that known as the Turbuhaler® in which a dosing unit meters the desired dose which is then inhaled by the patient. With this system the active compound, with or without a carrier substance, is delivered to the patient.

For oral administration the active compound may be admixed with an adjuvant or a carrier, for example, lactose, saccharose, sorbitol, mannitol; a starch, for example, potato starch,

corn starch or amylopectin; a cellulose derivative; a binder, for example, gelatine or polyvinylpyrrolidone; and/or a lubricant, for example, magnesium stearate, calcium stearate, polyethylene glycol, a wax, paraffin, and the like, and then compressed into tablets. If coated tablets are required, the cores, prepared as described above, may be coated with a concentrated sugar solution which may contain, for example, gum arabic, gelatine, talcum, titanium dioxide, and the like. Alternatively, the tablet may be coated with a suitable polymer dissolved in a readily volatile organic solvent.

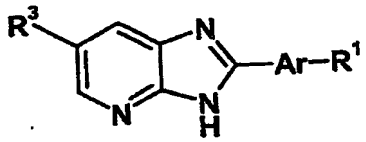
For the preparation of soft gelatine capsules, the compound may be admixed with, for example, a vegetable oil or polyethylene glycol. Hard gelatine capsules may contain granules of the compound using either the above mentioned excipients for tablets. Also liquid or semisolid formulations of the drug may be filled into hard gelatine capsules.

Liquid preparations for oral application may be in the form of syrups or suspensions, for example, solutions containing the compound, the balance being sugar and a mixture of ethanol, water, glycerol and propylene glycol. Optionally such liquid preparations may contain colouring agents, flavouring agents, saccharine and/or carboxymethylcellulose as a thickening agent or other excipients known to those skilled in art.

The compounds of the invention may also be administered in conjunction with other compounds used for the treatment of the above conditions.

Certain compounds of formula (I) are novel.

Therefore a further aspect of the invention provides a compound of formula (Ia)



(Ia)

wherein:

R^3 represents halogen, C1 to 3 alkyl or C1 to 3 alkoxy;

Ar represents phenyl, a 5- or 6-membered heteroaromatic ring or an indole ring; said heteroaromatic ring incorporating 1 to 3 heteroatoms independently selected from O, N and S; said phenyl, heteroaromatic or indole ring being optionally further substituted by chloro or OMe;

R^1 represents $(CH_2)_nNR^4R^5$ and n represents an integer 0 or 1;

R^4 represents H or C1 to 4 alkyl;

R^5 represents CH_2Ar^2;

Ar^2 represents phenyl, a 5- or 6-membered heteroaromatic ring or a benzimidazole ring; said heteroaromatic ring incorporating 1 to 3 heteroatoms independently selected from O, N and S; said phenyl, heteroaromatic or benzimidazole ring being optionally further substituted by one or two groups independently selected from halogen, C1 to 4 alkyl, CN, CH_2OH, C1 to 4 alkoxy, CO_2Me, CH_2OAc and pyridyl;

or a pharmaceutically acceptable salt thereof.

In one embodiment, R^1 in formula (Ia) represents $(CH_2)_nNR^4R^5$ and n represents the integer 0.

In one embodiment, R^3 in formula (Ia) represents halogen. In another embodiment, R^3 in formula (Ia) represents bromo.

In another embodiment, Ar in formula (Ia) represents phenyl.

Particular novel compounds of formula (Ia) include:

4-({[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]amino}methyl)benzonitrile

N-benzyl-N-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenyl]amine

N-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenyl]-N-(1H-imidazol-2-ylmethyl)amine

N-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenyl]-N-(1H-imidazol-5-ylmethyl)amine

3-({[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenyl]amino}methyl)benzonitrile

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(4-methoxybenzyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(2-methoxybenzyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(3-methoxybenzyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(2-chlorobenzyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(4-chlorobenzyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(1*H*-pyrazol-3-ylmethyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(3-chlorobenzyl)amine

[5-({[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]amino}methyl)-2-furyl]methanol

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(thien-2-ylmethyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(2-furylmethyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(thien-3-ylmethyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(4-methyl-1*H*-imidazol-5-yl)methyl]amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(3-furylmethyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(1,3-thiazol-2-ylmethyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(4-bromothien-2-yl)methyl]amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(1*H*-imidazol-4-ylmethyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(2-methyl-1*H*-imidazol-5-yl)methyl]amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(3,5-dimethylisoxazol-4-yl)methyl]amine

[5-({[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]amino}methyl)-2-furyl]methyl acetate

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(5-pyridin-2-ylthien-2-yl)methyl]amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(1-methyl-1*H*-benzimidazol-2-yl)methyl]amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(2-ethyl-1*H*-imidazol-5-yl)methyl]amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(1-methyl-1*H*-imidazol-5-yl)methyl]amine

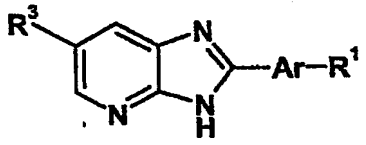
methyl 4-({[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]amino}methyl)-1-methyl-1*H*-pyrrole-2-carboxylate

N-benzyl-5-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)pyridin-2-amine

5-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)-*N*-(3-methoxybenzyl)pyridin-2-amine

and pharmaceutically acceptable salts thereof.

Another aspect of the invention provides a compound of formula (Ib)



(Ib)

wherein:

R^3 represents halogen, C1 to 3 alkyl or C1 to 3 alkoxy;

Ar represents phenyl, a 5- or 6-membered heteroaromatic ring or an indole ring; said heteroaromatic ring incorporating 1 to 3 heteroatoms independently selected from O, N and S; said phenyl, heteroaromatic or indole ring being optionally further substituted by chloro or OMe;

R^1 represents OR^2;

R^2 represents C3 to 4 alkyl substituted by NR^6R^7 and by OH;

R^6 represents H, C1 to 4 alkyl or $CH_2CH_2OCH_3$;

R^7 represents H, C1 to 6 alkyl, C3 to 6 cycloalkyl, Ar^3, a 5 or 6 membered saturated or partially unsaturated heterocyclic ring incorporating 1 or 2 heteroatoms selected independently from O, N and S and optionally substituted by Me, Et or CO_2Et; said C1 to 6 alkyl being optionally substituted by one or more groups selected independently from OH, CN, $CONMe_2$, CONHMe, C1 to 4 alkoxy, halogen, NMe_2, Ar^4, and a 5 or 6 membered saturated heterocyclic ring incorporating 1 or 2 heteroatoms selected independently from O, N and S and optionally also incorporating a carbonyl group; said C3 to 6 cycloalkyl being optionally substituted by OH or CN;

or the group $-NR^6R^7$ together represents a 5 to 7 membered saturated azacyclic ring optionally incorporating 1 additional heteroatom selected from O and NR^9; and optionally substituted by one or more substituents selected independently from OH, NMe_2, $CONH_2$, CH_2OH, CH_2CH_2OH, phenyl, pyridyl, piperidinyl and methoxyphenyl;

R^9 represents CH_2CH_2OH, $COCH_3$, Me, CO_2Et, CH_2CH_2OMe or a six membered aromatic or azaaromatic ring optionally further substituted by one or more substituents selected independently from Cl, CN, OMe and CF_3;

Ar^3 represents thiazolyl, triazolyl or tetrazolyl;

Ar^4 represents phenyl, a 5- or 6-membered heteroaromatic ring or an indole ring; said heteroaromatic ring incorporating 1 to 3 heteroatoms independently selected from O, N and S; said phenyl, heteroaromatic or indole ring being optionally further substituted by one or two groups independently selected from halogen and OMe;

or a pharmaceutically acceptable salt thereof.

In one embodiment, R^1 in formula (Ib) represents $OCH_2CHOHCH_2NR^6R^7$.

In one embodiment, R^3 in formula (Ib) represents halogen. In another embodiment, R^3 in formula (Ib) represents bromo.

In another embodiment, Ar in formula (Ib) represents phenyl.

Particular novel compounds of formula (Ib) include:

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-pyrrolidin-1-ylpropan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-morpholin-4-ylpropan-2-ol

1-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}pyrrolidin-3-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-piperidin-1-ylpropan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-(diethylamino)propan-2-ol

1-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}piperidin-4-ol

1-(4-acetylpiperazin-1-yl)-3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[3-(dimethylamino)pyrrolidin-1-yl]propan-2-ol

4-[({2-hydroxy-3-[4-(6-methyl-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]propyl}amino)methyl]phenol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(2-hydroxyethyl)(methyl)amino]propan-2-ol

3-[{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}(methyl)amino]propanenitrile

4-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}piperazin-1-ol

N^2-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}-N^1,N^1,N^2-trimethylglycinamide

1-[benzyl(methyl)amino]-3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[methyl(2-phenylethyl)amino]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-(4-phenylpiperazin-1-yl)propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-(4-pyridin-2-ylpiperazin-1-yl)propan-2-ol

1-[2-({3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}amino)ethyl]imidazolidin-2-one

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(3-methoxybenzyl)amino]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(2-chlorobenzyl)amino]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(4-chlorobenzyl)amino]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(3-chlorobenzyl)amino]propan-2-ol

ethyl 4-({3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}amino)piperidine-1-carboxylate

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[4-(2-methoxyethyl)piperazin-1-yl]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-(cyclopropylamino)propan-2-ol

3-({3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}amino)propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(2-methoxyethyl)amino]propan-2-ol

2-({3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}amino)propan-1-ol

1-(benzylamino)-3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(pyridin-3-ylmethyl)amino]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(pyridin-4-ylmethyl)amino]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(1-ethylpiperidin-3-yl)amino]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(2-morpholin-4-ylethyl)amino]propan-2-ol

1-[3-({3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}amino)propyl]pyrrolidin-2-one

1-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}piperidin-3-ol

1-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}prolinamide

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[4-(hydroxymethyl)piperidin-1-yl]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[2-(hydroxymethyl)piperidin-1-yl]propan-2-ol

1-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}piperidine-4-carboxamide

1-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}piperidine-3-carboxamide

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[4-(2-hydroxyethyl)piperazin-1-yl]propan-2-ol

2-(4-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}piperazin-1-yl)benzonitrile

6-(4-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}piperazin-1-yl)nicotinonitrile

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-(1,3-thiazol-2-ylamino)propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-(4-pyrazin-2-ylpiperazin-1-yl)propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(2-methoxybenzyl)amino]propan-2-ol

4-[{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}(methyl)amino]cyclohexanecarbonitrile

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-(2-pyridin-3-ylpiperidin-1-yl)propan-2-ol

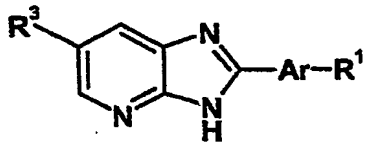
1-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}-4-phenylpiperidin-4-ol

2-({3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}amino)-3-methylbutan-1-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[4-(3-methoxyphenyl)piperazin-1-yl]propan-2-ol

and pharmaceutically acceptable salts thereof.

Another aspect of the invention provides a compound of formula (Ic)



(Ic)

wherein:

R^3 represents halogen, C1 to 3 alkyl or C1 to 3 alkoxy;

Ar represents phenyl, a 5- or 6-membered heteroaromatic ring or an indole ring; said heteroaromatic ring incorporating 1 to 3 heteroatoms independently selected from O, N and S; said phenyl, heteroaromatic or indole ring being optionally further substituted by chloro or OMe;

R^1 represents OR^2;

R^2 represents C2 to 4 alkyl substituted by a group NR^6R^7;

R^6 represents H, C1 to 4 alkyl or $CH_2CH_2OCH_3$;

R^7 represents H, C1 to 6 alkyl, C3 to 6 cycloalkyl, Ar^3, a 5 or 6 membered saturated or partially unsaturated heterocyclic ring incorporating 1 or 2 heteroatoms selected independently from O, N and S and optionally substituted by Me, Et or CO_2Et; said C1 to 6 alkyl being optionally substituted by one or more groups selected independently from OH, CN, $CONMe_2$, CONHMe, C1 to 4 alkoxy, halogen, NMe_2, Ar^4, and a 5 or 6 membered saturated heterocyclic ring incorporating 1 or 2 heteroatoms selected independently from O, N and S and optionally also incorporating a carbonyl group; said C3 to 6 cycloalkyl being optionally substituted by OH or CN;

or the group $-NR^6R^7$ together represents a 5 or 6 membered saturated azacyclic ring optionally incorporating 1 additional heteroatom selected from O and NR^9; and optionally substituted by one or more substituents selected independently from OH, NMe_2, $CONH_2$, CH_2OH, CH_2CH_2OH, phenyl, pyridyl, piperidinyl or methoxyphenyl;

R^9 represents CH_2CH_2OH, $COCH_3$, Me, CO_2Et, CH_2CH_2OMe or a six membered aromatic or azaaromatic ring optionally further substituted by one or more substituents selected independently from Cl, CN, OMe and CF_3;

Ar^3 represents thiazolyl, triazolyl or tetrazolyl;

Ar^4 represents phenyl, a 5- or 6-membered heteroaromatic ring or an indole ring; said heteroaromatic ring incorporating 1 to 3 heteroatoms independently selected from O, N and S; said phenyl, heteroaromatic or indole ring being optionally further substituted by one or two groups independently selected from halogen and OMe;

or a pharmaceutically acceptable salt thereof,
with the provisos that:
i) when R^6 represents H or C1 to 4 alkyl, R^3 does not represent unsubstituted C1 to 4 alkyl; and
ii) that the group $-NR^6R^7$ does not represent unsubstituted morpholine, thiomorpholine, 4-methylpiperazine or 4-phenylpiperazine.

In one embodiment, R^3 in formula (Ic) represents halogen. In another embodiment, R^3 in formula (Ic) represents bromo.

In another embodiment, Ar in formula (Ic) represents phenyl.

Particular novel compounds of formula (Ic) include:

6-bromo-2-[4-(2-{4-[3-chloro-5-(trifluoromethyl)pyridin-2-yl]piperazin-1-yl}ethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine

6-bromo-2-[4-(2-piperidin-1-ylethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine

6-bromo-2-[4-(3-piperidin-1-ylpropoxy)phenyl]-3H-imidazo[4,5-b]pyridine

6-bromo-2-[4-(3-pyrrolidin-1-ylpropoxy)phenyl]-3H-imidazo[4,5-b]pyridine

N-{2-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]ethyl}-*N*-(tetrahydrofuran-2-ylmethyl)amine

6-bromo-2-[4-(2-pyrrolidin-1-ylethoxy)phenyl]-3H-imidazo[4,5-b]pyridine

2-[{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}(methyl)amino]ethanol

3-[{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}(methyl)amino]propanenitrile

1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}pyrrolidin-3-ol

1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N,N-dimethylpyrrolidin-3-amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N,1-dimethylpyrrolidin-3-amine

N^2-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N^1,N^1,N^2-trimethylglycinamide

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-ethyl-N',N'-dimethylethane-1,2-diamine

N-benzyl-N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-methylamine

2-{4-[2-(4-acetylpiperazin-1-yl)ethoxy]phenyl}-6-bromo-3H-imidazo[4,5-b]pyridine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N,N-bis(2-methoxyethyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-methyl-N-(2-phenylethyl)amine

6-bromo-2-{4-[2-(4-pyridin-2-ylpiperazin-1-yl)ethoxy]phenyl}-3H-imidazo[4,5-b]pyridine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-[3-(1H-imidazol-1-yl)propyl]amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(4-methoxybenzyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(3-methoxybenzyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(4-chlorobenzyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(3-chlorobenzyl)amine

ethyl 4-({2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}amino)piperidine-1-carboxylate

6-bromo-2-(4-{2-[4-(2-methoxyethyl)piperazin-1-yl]ethoxy}phenyl)-3H-imidazo[4,5-b]pyridine

1-({2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}amino)propan-2-ol

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(2-methoxyethyl)amine

2-({2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}amino)propan-1-ol

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(2-furylmethyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(tetrahydrofuran-2-ylmethyl)amine

N-benzyl-N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(pyridin-3-ylmethyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(pyridin-4-ylmethyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(thien-2-ylmethyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(1-phenylethyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-1-ethylpiperidin-3-amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(2-morpholin-4-ylethyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(2-methoxybenzyl)amine

1-[3-({2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}amino)propyl]pyrrolidin-2-one

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-[2-(4-chlorophenyl)ethyl]amine

4-[{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}(methyl)amino]cyclohexanecarbonitrile

1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperidin-3-ol

6-bromo-2-{4-[2-(2-pyridin-3-ylpiperidin-1-yl)ethoxy]phenyl}-3H-imidazo[4,5-b]pyridine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-cyclopentylamine

1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-4-phenylpiperidin-4-ol

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-[2-(1H-imidazol-4-yl)ethyl]amine

1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperidine-3-carboxamide

6-bromo-2-{4-[2-(4-pyrazin-2-ylpiperazin-1-yl)ethoxy]phenyl}-3H-imidazo[4,5-b]pyridine

(1*S*,2*S*)-2-({2-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]ethyl}amino)cyclohexanol

6-bromo-2-(4-{2-[4-(3-methoxyphenyl)piperazin-1-yl]ethoxy}phenyl)-3H-imidazo[4,5-b]pyridine

(1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperidin-4-yl)methanol

4-({2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}amino)cyclohexanol

(1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperidin-2-yl)methanol

1'-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-1,4'-bipiperidine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-1,3-thiazol-2-amine

1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperidine-4-carboxamide

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-1H-1,2,4-triazol-3-amine

2-(4-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperazin-1-yl)benzonitrile

6-(4-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperazin-1-yl)nicotinonitrile

1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}prolinamide

6-bromo-2-(4-{2-[4-(2-methoxyphenyl)piperidin-1-yl]ethoxy}phenyl)-3H-imidazo[4,5-b]pyridine

2-(4-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperazin-1-yl)ethanol

1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperidin-4-ol

6-bromo-2-(4-{2-[4-(2-methoxyphenyl)piperazin-1-yl]ethoxy}phenyl)-3H-imidazo[4,5-b]pyridine

(2*S*)-2-({2-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]ethyl}amino)-3-methylbutan-1-ol

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-4,5-dihydro-1,3-thiazol-2-amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-[2-(1H-indol-3-yl)ethyl]amine

(2*S*)-2-({2-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]ethyl}amino)-2-phenylethanol

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-1H-tetrazol-5-amine

(1*S*,2*R*)-2-({2-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]ethyl}amino)cyclohexanol

and pharmaceutically acceptable salts thereof.

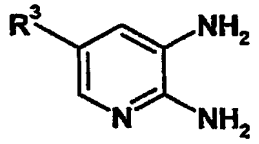
According to the invention there is also provided a compound of formula (Ia), (Ib) or (Ic) or a pharmaceutically acceptable salt thereof, for use as a medicament.

The present invention includes compounds of formulae (I) and (Ia) and (Ib) and (Ic) in the form of salts, in particular acid addition salts. Suitable salts include those formed with both

organic and inorganic acids. Such acid addition salts will normally be pharmaceutically acceptable although salts of non-pharmaceutically acceptable acids may be of utility in the preparation and purification of the compound in question. Thus, preferred salts include those formed from hydrochloric, hydrobromic, sulphuric, phosphoric, citric, tartaric, lactic, pyruvic, acetic, succinic, fumaric, maleic, methanesulphonic and benzenesulphonic acids.

In a further aspect the invention provides a process for the preparation of a compound of formula (Ia), (Ib) or (Ic) which comprises:

a) reaction of a compound of the general formula (II):



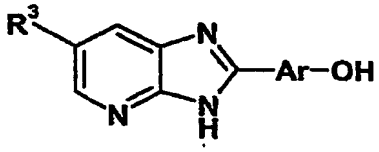
(II)

in which R^3 is as defined in formula (Ia), (Ib) or (Ic),
with a compound of formula (III):

$$R^1\text{-Ar-CHO} \quad \text{(III)}$$

in which R^1 and Ar are as defined in formula (Ia), (Ib) or (Ic), in the presence of an oxidizing agent; or

b) reaction of a compound of formula (IV):



(IV)

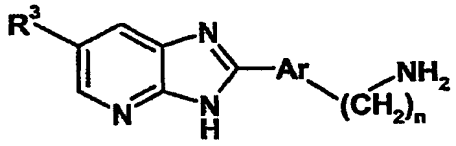
in which R^3 and Ar are as defined in formula (Ib) or (Ic);

with a compound of formula (V):

$$R^2\text{-LG} \qquad (V)$$

in which R^2 is as defined in formula (Ib) or (Ic) and LG represents a leaving group; or

c) reaction of a compound of the general formula (VI):



(VI)

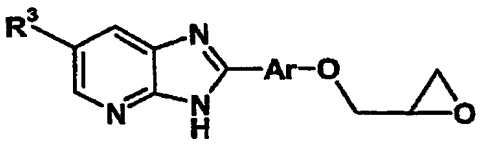
in which n, R^3 and Ar are as defined in formula (Ia);

with a compound of formula (VII):

$$Ar^2\text{-CHO} \qquad (VII)$$

in which Ar^2 is as defined in formula (Ia), or

d) reaction of a compound of the general formula (VIII):



(VIII)

in which R^3 and Ar are as defined in formula (Ib);

with a compound of formula (IX):

$$HNR^6R^7 \qquad (IX)$$

in which R^6 and R^7 are as defined in formula (Ib)

and where desired or necessary converting the resultant compound of formula (Ia), (Ib) or (Ic) or another salt thereof, into a pharmaceutically acceptable salt thereof; or converting one compound of formula (Ia), (Ib) or (Ic) into another compound of formula (Ia), (Ib) or (Ic); and where desired converting the resultant compound of formula (Ia), (Ib) or (Ic) into an optical isomer thereof.

In process (a), the reaction is carried out in the presence of a suitable oxidising agent, for example, iron(III) chloride, and air is continuously bubbled through the reaction solution. Suitable solvents include N,N-dimethylformamide. The reaction is generally carried out at an elevated temperature up to the boiling point of the solvent and for a sufficient length of time for the reaction to go to completion. When the reaction is conducted in N,N-dimethylformamide at about 120 °C, typical reaction times are from 2 to 20 hours.

In process (b), the reaction is generally carried out in the presence of a suitable base, for example, sodium hydride, and in a suitable organic solvent, for example, N,N-dimethylformamide.

In process (c), the reaction is carried out in the presence of a suitable reducing agent, for example, sodium triacetoxyborohydride or catalytic hydrogenation.

In process (d), the reaction is carried out in a suitable organic solvent, for example, N,N-dimethylformamide, at a suitable temperature between room temperature and the boiling point of the solvent.

It will be appreciated that in the above processes, certain functional groups may need to be protected using standard protecting groups. The protection and deprotection of functional groups is, for example, described in 'Protective Groups in Organic Chemistry', edited by J. W. F. McOmie, Plenum Press (1973), and 'Protective Groups in Organic Synthesis', 3rd edition, T. W. Greene & P. G. M. Wuts, Wiley–Interscience (1999).

Compounds of the general formula (VIII) may be prepared by reacting a compound of the general formula (IV) with a compound of the general (V) in which R^2 is 2,3-epoxypropyl.

Salts of compounds of formula (I) may be formed by reacting the free base or a salt, enantiomer, tautomer or protected derivative thereof, with one or more equivalents of the appropriate acid. The reaction may be carried out in a solvent or medium in which the salt is insoluble, or in a solvent in which the salt is soluble followed by subsequent removal of the solvent *in vacuo* or by freeze drying. Suitable solvents include, for example, water, dioxan, ethanol, 2-propanol, tetrahydrofuran or diethyl ether, or mixtures thereof. The reaction may be a metathetical process or it may be carried out on an ion exchange resin.

The compounds of the invention and intermediates may be isolated from their reaction mixtures, and if necessary further purified, by using standard techniques.

The compounds of formula (Ia), (Ib) and (Ic) may exist in enantiomeric or diastereoisomeric forms or mixtures thereof, all of which are included within the scope of the invention. The various optical isomers may be isolated by separation of a racemic mixture of the compounds using conventional techniques, for example, fractional crystallisation or HPLC. Alternatively, the individual enantiomers may be made by reaction of the appropriate optically active starting materials under reaction conditions that will not cause racemisation.

Intermediate compounds may also exist in enantiomeric forms and may be used as purified enantiomers, diastereomers, racemates or mixtures thereof.

The compounds of formula (Ia), (Ib) and (Ic) and their pharmaceutically acceptable salts, enantiomers, racemates and tautomers, are useful because they possess pharmacological activity in animals. The compounds of formula (Ia), (Ib) and (Ic) have activity as pharmaceuticals, in particular as modulators of kinase activity, especially Itk kinase activity, and as such are predicted to be useful in therapy. They may be used in the treatment or prophylaxis of allergic, autoimmune, inflammatory, proliferative and hyperproliferative diseases and immune-mediated diseases including rejection of transplanted organs or tissues and Acquired Immunodeficiency Syndrome (AIDS).

Examples of these medical conditions are disclosed above.

The compounds of formula (Ia), (Ib) and (Ic) may be used on their own, or in the form of appropriate pharmaceutical formulations comprising the compound of the invention in combination with a pharmaceutically acceptable diluent, adjuvant or carrier. Particularly preferred are compositions not containing material capable of causing an adverse reaction, for example, an allergic reaction. Conventional procedures for the selection and preparation of suitable pharmaceutical formulations are described in, for example, "Pharmaceuticals - The Science of Dosage Form Designs", M. E. Aulton, Churchill Livingstone, 1988.

In another aspect the invention provides a pharmaceutical formulation comprising a therapeutically effective amount of a compound of formula (Ia), (Ib) or (Ic), or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

The following Examples are intended to illustrate, but in no way limit the scope of the invention.

General methods All reactions were performed in dried glassware in an argon atmosphere at room temperature, unless otherwise noted. All reagents and solvents were used as received. Merck Silica gel 60 (0.040-0.063 mm) was used for preparative silica gel

chromatography. A Kromasil KR-100-5-C18 column (250 x 20 mm, Akzo Nobel) and mixtures of acetonitrile/water at a flow rate of 10 ml/min were used for preparative HPLC. Reactions were monitored at 254 nm by analytical HPLC, using a Kromasil C-18 column (150 x 4.6 mm) and a gradient (containing 0.1% trifluoroacetic acid) of 5 to 100% of acetonitrile in water at a flow rate of 1 ml/min. Evaporations of solvents were performed under reduced pressure using a rotary evaporator at a maximum temperature of 60 °C. Products were dried under reduced pressure at 40 °C.

^{1}H-NMR spectra were recorded on a Varian Inova 400 MHz or Varian Mercury 300 MHz instrument. The central solvent peak of chloroform-*d* (δ_H 7.27 ppm), dimethylsulfoxide-d_6 (δ_H 2.50 ppm) or methanol-d_4 (δ_H 3.35 ppm) were used as internal references. Low resolution mass spectra obtained on a Hewlett Packard 1100 LC-MS system equipped with a APCI ionisation chamber.

Preparation 1

5-Bromo-2,3-diaminopyridine

The title compound was prepared essentially as described by Petrow. et al., *J.Chem.Soc.* (1948) 1389, 1391.

A mixture of 2-amino-5-bromo-3-nitropyridine (62.2 g, 285 mmol), iron powder (171 g, 3.06 mol), concentrated hydrochloric acid (2.85 ml), water (60 ml) and ethanol (230 ml) was refluxed for 2 h, filtered whilst warm, the solids washed twice with ethanol (2 x 150 ml) and the combined ethanol solutions were evaporated to dryness. The crude solid was recrystallized from water, using decolourising charcoal, filtered whilst warm, the solids washed twice with warm ethanol (2 x 100 ml), the ethanol evaporated off and the precipitate was filtered off, washed with water (3 x 75 ml) and dried to afford the title compound (27 g, 50%).

^{1}H NMR (DMSO-d_6): δ 7.26 (1H, d); 6.78 (1H, d); 5.57 (2H, s); 4.97 (2H, s).

APCI-MS m/z: 188.1/190.1 [MH^+].

Example 1

4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenol

A mixture of 5-bromo-2,3-diaminopyridine (11.3 g, 60 mmol), 4-hydroxybenzaldehyde (7.3 g, 60 mmol) and iron(III) chloride hexahydrate (0.48 g, 1.8 mmol) in DMF (200 ml) was heated to 120 °C with air bubbling continuously through the solution until the reaction was complete (typical reaction time 4 to 16 h).
The reaction mixture was poured into ice-water, filtered and the solids washed with water, ethanol, methanol and then dried. The solids were recrystallized twice from DMF (250 ml then 150 ml), filtered, washed with methanol, diethyl ether and dried to afford the title compound (11.3 g, 65%).

^{1}H NMR (DMSO-d_6): δ 13.36 (1H, brs); 10.12 (1H, brs); 8.33 (1H, s); 8.15 (1H, s); 8.05 (2H, d); 6.91 (2H, d).
APCI-MS m/z: 290.1/292 [MH^+].

Following the general method of Example 1, the compounds of Examples 2 to 38 were prepared:

Example 2

N-{3-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]propyl}-*N*,*N*-dimethylamine

The title compound was prepared from 5-bromo-2,3-diaminopyridine (376 mg, 2 mmol) and 4-[3-(dimethylamino)-propoxy]benzaldehyde (420 mg, 2 mmol).

^{1}H NMR (DMSO-d_6): δ 13.39 (1H, brs); 8.35 (1H, d); 8.19 (1H, brs); 8.15 (2H, d); 7.11 (2H, d); 4.08 (2H, t); 2.36 (2H, t); 2.14 (6H, s); 1.87 (2H, qv).
APCI-MS m/z: 375.2/377.1 [MH^+].

Example 3

6-Bromo-2-{4-[(5-chloro-1,2,3-thiadiazol-4-yl)methoxy]phenyl}-3*H*-imidazo[4,5-*b*]pyridine

The title compound was prepared from 5-bromo-2,3-diaminopyridine and 4-[(5-chloro-1,2,3-thiadiazol-4-yl)methoxy]benzaldehyde.

^{1}H NMR (DMSO-d_6): δ 13.50 (1H, brs); 8.37 (1H, d); 8.21 (1H, brs); 8.20 (2H, d); 7.30 (2H, d); 5.59 (2H, s).

APCI-MS m/z: 422/424 [MH^+].

Example 4

6-Bromo-2-{4-[(2-chloro-1,3-thiazol-5-yl)methoxy]phenyl}-3*H*-imidazo[4,5-*b*]pyridine

The title compound was prepared from 5-bromo-2,3-diaminopyridine and 4-[(2-chloro-1,3-thiazol-5-yl)methoxy]benzaldehyde.

^{1}H NMR (DMSO-d_6): δ 13.47 (1H, brs); 8.36 (1H, d); 8.20 (1H, brs); 8.17 (2H, d); 7.84 (1H, s); 7.22 (2H, d); 5.54 (2H, s).

APCI-MS m/z: 421/423 [MH^+].

Example 5

6-Bromo-2-[4-(2-{4-[3-chloro-5-(trifluoromethyl)pyridin-2-yl]piperazin-1-yl}ethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine

The title compound was prepared from 5-bromo-2,3-diaminopyridine and 4-(2-[4-[3-chloro-5-(trifluoromethyl)-2-pyridinyl]piperazino]ethoxy)]benzaldehyde.

^{1}H NMR (DMSO-d_6): δ 13.45 (1H, brs); 8.54 (1H, d); 8.35 (1H, d); 8.19 (1H, brs); 8.17 (1H, brs); 8.15 (2H, d); 7.15 (2H, d); 4.22 (2H, t); 3.46 (4H, brt); 2.80 (2H, t); 2.66 (4H, brt).

APCI-MS m/z: 581.1/583.1 [MH^+].

Example 6

6-Bromo-2-[4-(2-piperidin-1-ylethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine

The title compound was prepared from 5-bromo-2,3-diaminopyridine and 4-[2-(1-piperidinyl)ethoxy]benzaldehyde.

^{1}H NMR (DMSO-d_6): δ 13.41 (1H, brs); 8.35 (1H, d); 8.19 (1H, brs); 8.15 (2H, d); 7.12 (2H, d); 4.16 (2H, t); 2.67 (2H, t); 2.43 (4H, brt); 1.49 (4H, m); 1.38 (2H, m).

APCI-MS m/z: 401.1/403.1 [MH^+].

Example 7

[5-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)-2-furyl]methanol

The title compound was prepared from 5-bromo-2,3-diaminopyridine and 5-hydroxymethyl-2-furaldehyde.

^{1}H NMR (DMSO-d_6): δ 13.58 (1H, brs); 8.38 (1H, d); 8.17 (1H, brs); 7.28 (1H, d); 6.57 (1H, d); 5.43 (1H, t); 4.52 (2H, d).

APCI-MS m/z: 294/296 [MH^+].

Example 8

6-Bromo-2-(7-methyl-1H-indol-3-yl)-3H-imidazo[4,5-b]pyridine

The title compound was prepared from 5-bromo-2,3-diaminopyridine and 7-methylindole-3-carboxaldehyde.

^{1}H NMR (DMSO-d_6): δ 13.11 (1H, brs); 11.81 (1H, s); 8.31 (1H, s); 8.29-8.24 (2H, m); 8.13 (1H, brs); 7.11 (1H, t); 7.02 (1H, brd); 2.51 (3H, s).

APCI-MS m/z: 327/329 [MH^+].

Example 9

6-Bromo-2-(1-phenyl-1H-1,2,3-triazol-4-yl)-3H-imidazo[4,5-b]pyridine

The title compound was prepared from 5-bromo-2,3-diaminopyridine and 1-phenyl-1H-1,2,3-triazole-4-carboxaldehyde.

^{1}H NMR (DMSO-d_6): δ 13.66 (1H, brs); 9.60 (1H, s); 8.42 (1H, d); 8.20 (1H, brs); 8.02 (2H, d); 7.68-7.51 (3H, m).

APCI-MS m/z: 341/343 [MH^+].

Example 10

6-Bromo-2-(1H-pyrrol-2-yl)-3H-imidazo[4,5-b]pyridine

The title compound was prepared from 5-bromo-2,3-diaminopyridine and pyrrole-2-carboxaldehyde.

^{1}H NMR (DMSO-d_6): δ 13.11 (1H, brs); 12.00 (1H, s); 8.27 (1H, d); 8.06 (1H, s); 6.99 (2H, m); 6.21 (1H, m).

APCI-MS m/z: 263/265 [MH^+].

Example 11

6-Bromo-2-(1H-pyrazol-3-yl)-3H-imidazo[4,5-b]pyridine

The title compound was prepared from 5-bromo-2,3-diaminopyridine and pyrazole-3-carbaldehyde.

^{1}H NMR (DMSO-d_6): δ 13.49 (2H, brs); 8.37 (1H, s); 8.15 (1H, brs); 7.92 (1H, s); 6.94 (1H, d).

APCI-MS m/z: 264/266 [MH^+].

Example 12

6-Bromo-2-(4-bromo-1H-pyrazol-3-yl)-3H-imidazo[4,5-b]pyridine

The title compound was prepared from 5-bromo-2,3-diaminopyridine and 4-bromo-1H-pyrazole-5-carbaldehyde.

^{1}H NMR (DMSO-d_6): δ 13.76 (2H, brs); 8.42 (1H, s); 8.22 (2H, brs).

APCI-MS m/z: 341.9/343.9/345.9 [MH^+].

Example 13

6-Bromo-2-(2-methyl-1H-imidazol-5-yl)-3H-imidazo[4,5-b]pyridine

The title compound was prepared from 5-bromo-2,3-diaminopyridine 2-methyl-1H-imidazole-4-carbaldehyde.

^{1}H NMR (DMSO-d_6/D_2O): δ 8.29 (1H, s); 8.06 (1H, s); 7.78 (1H, s); 2.34 (3H, s).

APCI-MS m/z: 278/280 [MH^+].

Example 14

4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)-2-methoxyphenol

The title compound was prepared from 5-bromo-2,3-diaminopyridine and 4-hydroxy-3-methoxybenzaldehyde.

^{1}H NMR (DMSO-d_6): δ 13.35 (1H, brs); 9.71 (1H, brs); 8.33 (1H, d); 8.16 (1H, brs); 7.77 (1H, d); 7.67 (1H, dd); 6.91 (1H, d); 3.87 (3H, s).
APCI-MS m/z: 320/322 [MH^+].

Example 15

4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)-2-chlorophenol

The title compound was prepared from 5-bromo-2,3-diaminopyridine and 3-chloro-4-hydroxybenzaldehyde.

^{1}H NMR (DMSO-d_6): δ 13.54 (1H, brs); 10.92 (1H, brs); 8.36 (1H, s); 8.22 (1H, brs); 8.20 (1H, d); 8.01 (1H, dd); 7.12 (1H, d).
APCI-MS m/z: 323.9/325.9 [MH^+].

Example 16

4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)-3-methoxyphenol

The title compound was prepared from 5-bromo-2,3-diaminopyridine and 4-hydroxy-2-methoxybenzaldehyde.

^{1}H NMR (DMSO-d_6): δ 12.58 (NH-tautomer, s); 12.06 (NH-tautomer, s); 10.22 (1H, s); 8.39-7.96 (3H, m); 6.57 (2H, m); 3.96 (3H, brd).
APCI-MS m/z: 320/322 [MH^+].

Example 17

4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)-3-chlorophenol

The title compound was prepared from 5-bromo-2,3-diaminopyridine and 2-chloro-4-hydroxybenzaldehyde.

^{1}H NMR (DMSO-d_6): δ 13.15 (1H, brs); 10.53 (1H, brs); 8.41 (1H, d); 8.23 (1H, brs); 7.73 (1H, d); 6.99 (1H, d); 6.90 (1H, dd).

APCI-MS m/z: 323.9/325.9 [MH^+].

Example 18

N-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)-3-methoxyphenyl]-N,N-dimethylamine

The title compound was prepared from 5-bromo-2,3-diaminopyridine and 4-dimethylamino-2-methoxybenzaldehyde.

^{1}H NMR (DMSO-d_6): δ 12.04 (1H, brs); 8.29 (1H, s); 8.12 (1H, d); 8.01 (1H, brs); 6.47 (1H, d); 6.35 (1H, s); 4.00 (3H, s); 3.03 (6H, s).

APCI-MS m/z: 347/349 [MH^+].

Example 19

2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethanol

The title compound was prepared from 5-bromo-2,3-diaminopyridine and 4-(2-hydroxyethoxy)benzaldehyde.

^{1}H NMR (DMSO-d_6): δ 13.46 (1H, brs); 8.36 (1H, d); 8.19 (1H, brs); 8.15 (2H, d); 7.13 (2H, d); 4.90 (1H, t); 4.08 (2H, t); 3.74 (2H, m).

APCI-MS m/z: 334/336 [MH^+].

Example 20

6-Bromo-2-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridine trifluoroacetate

The title compound was prepared from 5-bromo-2,3-diaminopyridine (0.060 g, 0.3 mmol) and 3-fluorobenzaldehyde (0.037 g, 0.30 mmol). The product was purified by RP-HPLC (10-60 % acetonitrile).

^{1}H NMR (CD_3OD): δ 8.42 (1H, brs); 8.29 (1H, brs); 8.02 (2H, brd); 7.61 (1H, brd); 7.39 (1H, brd).

APCI-MS m/z: 292.0 /294.0 [MH^+].

Example 21

6-Bromo-2-(2-methylphenyl)-3H-imidazo[4,5-b]pyridine trifluoroacetate

The title compound was prepared from 5-bromo-2,3-diaminopyridine (0.060 g, 0.32 mmol) and 2-methylbenzaldehyde (0.036 g, 0.30 mmol).

^{1}H NMR (CD_3OD): δ 8.44 (1H, brs); 8.17 (1H, brs); 7.65 (1H, brd); 7.43-7.34 (3H, m); 2.54 (3H, s).

APCI-MS m/z: 288.0/290 [MH^+].

Example 22

6-Bromo-2-(2-methoxyphenyl)-3H-imidazo[4,5-b]pyridine trifluoroacetate

The title compound was prepared from 5-bromo-2,3-diaminopyridine (0.060 g, 0.32 mmol) and 2-methoxybenzaldehyde (0.041 g, 0.30 mmol).

^{1}H NMR (CD_3OD): δ 8.52 (1H, brs); 8.22 (1H, brs); 8.16 (1H, brd); 7.62 (1H, t); 7.27 (1H, brd); 7.17 (1H, t); 4.09 (3H, s).

APCI-MS m/z: 304.0/306.0 [MH^+].

Example 23

6-Bromo-2-(4-isopropoxyphenyl)-3H-imidazo[4,5-b]pyridine trifluoroacetate

The title compound was prepared from 5-bromo-2,3-diaminopyridine (0.060 g, 0.32 mmol) and 4-isopropoxybenzaldehyde (0.049 g, 0.30 mmol).

^{1}H NMR (DMSO-d_6): δ 8.36 (1H, brs); 8.20 (1H, brs); 8.15 (2H, brd); 7.10 (2H, brd); 4.75 (1H, m); 1.31 (6H, d).

APCI-MS m/z: 332.0/334.0 [MH^+].

Example 24

4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)benzonitrile trifluoroacetate

The title compound was prepared from 5-bromo-2,3-diaminopyridine (0.060 g, 0.32 mmol) and 4-cyanobenzaldehyde (0.039 g, 0.30 mmol).

^{1}H NMR (DMSO-d_6): δ 8.52-8.39 (3H, m); 8.25 (1H, brs); 8.07 (2H, brd).

APCI-MS m/z: 299.2/301.0 [MH^+].

Example 25

2-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenol trifluoroacetate

The title compound was prepared from 5-bromo-2,3-diaminopyridine (0.060 g, 0.32 mmol) and salicylaldehyde (0.037 g, 0.30 mmol).

^{1}H NMR (CD_3OD): δ 8.49 (1H, brs); 8.21 (1H, brs); 8.14 (1H, brd); 7.45 (1H, t); 7.06 (2H, m).

APCI-MS m/z: 290.0/292.0 [MH^+].

Example 26

6-Bromo-2-(4-isopropylphenyl)-3H-imidazo[4,5-b]pyridine trifluoroacetate

The title compound was prepared from 5-bromo-2,3-diaminopyridine (0.060 g, 0.32 mmol) and 4-isopropylbenzaldehyde (0.044 g, 0.30 mmol).

^{1}H NMR (DMSO-d_6): δ 8.40 (1H, brd); 8.25 (1H, brs); 8.15 (2H, brd); 7.46 (2H, brd); 2.98 (1H, m); 1.25 (6H, d).

APCI-MS m/z: 316.0/318.0 [MH^+].

Example 27

6-Bromo-2-(4-methoxyphenyl)-3H-imidazo[4,5-b]pyridine trifluoroacetate

The title compound was prepared from 5-bromo-2,3-diaminopyridine (0.060 g, 0.32 mmol) and 4-methoxybenzaldehyde (0.041 g, 0.30 mmol).

^{1}H NMR (DMSO-d_6): δ 8.38 (1H, brs); 8.21 (1H, brs); 8.18 (2H, brd); 7.14 (2H, brd); 3.85 (3H, s).

APCI-MS m/z: 304.0/306.0 [MH^+].

Example 28

6-Bromo-2-(3-methoxyphenyl)-3H-imidazo[4,5-b]pyridine trifluoroacetate

The title compound was prepared from 5-bromo-2,3-diaminopyridine (0.060 g, 0.32 mmol) and 3-methoxybenzaldehyde (0.041 g, 0.30 mmol).

^{1}H NMR (DMSO-d_6): δ 8.43 (1H, d); 8.29 (1H, brs); 7.83(1H, brs); 7.79 (1H, brd); 7.49 (1H, t); 7.13 (1H, brd); 3.87 (3H, s).
APCI-MS m/z: 304.0/306.0 [MH^+].

Example 29

2-[4-(Benzyloxy)-3-methoxyphenyl]-6-bromo-3H-imidazo[4,5-b]pyridine trifluoroacetate

The title compound was prepared from 5-bromo-2,3-diaminopyridine (0.060 g, 0.32 mmol) and 4-benzyloxy -3-methoxybenzaldehyde (0.072 g, 0.30 mmol).

^{1}H NMR (CD_3OD): δ 8.46 (1H, brd); 8.16 (1H, d); 7.80 (1H, d); 7.71 (1H, dd); 7.48 (2H, brd); 7.42-7.32 (3H, m); 7.21 (2H, d); 5.23 (2H, s); 3.99 (3H, s).
APCI-MS m/z: 410.0/412.0 [MH^+].

Example 30

6-Bromo-2-thien-3-yl-3H-imidazo[4,5-b]pyridine trifluoroacetate

The title compound was prepared from 5-bromo-2,3-diaminopyridine (0.060 g, 0.32 mmol) and 3-thiophenecarboxaldehyde (0.034 g, 0.30 mmol).

^{1}H NMR (CD_3OD): δ 8.47 (1H, d); 8.33 (1H, m); 8.18 (1H, d); 7.81 (1H, dd); 7.69 (1H, dd).
APCI-MS m/z: 280.2/282.2 [MH^+].

Example 31

6-Bromo-2-(4-tert-butylphenyl)-1H-imidazo[4,5-b]pyridine trifluoroacetate

The title compound was prepared from 5-bromo-2,3-diaminopyridine and 4-*tert*-butylbenzaldehyde.

APCI-MS m/z: 343.3/345.3 [MH^+].

Example 32

N-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenyl]-N,N-dimethylamine bis(trifluoroacetate)

The title compound was prepared from 5-bromo-2,3-diaminopyridine (0.060 g, 0.32 mmol) and 4-dimethylaminobenzaldehyde (0.045 g, 0.30 mmol).

^{1}H NMR (CD_3OD): δ 8.38 (1H, brs); 8.06 (1H, d); 7.97 (2H, brd); 6.88 (2H, brd); 3.09 (6H, s).

APCI-MS m/z: 330.3/332.3 [MH^+].

Example 33

6-Bromo-2-(4-pyrrolidin-1-ylphenyl)-3H-imidazo[4,5-b]pyridine bis(trifluoroacetate)

The title compound was prepared from 5-bromo-2,3-diaminopyridine and 4-(1-pyrrolidino)benzaldehyde.

^{1}H NMR (CD_3OD): δ 8.44 (1H, d); 8.11 (1H, d); 7.97 (2H, dd); 6.76 (2H, dd); 3.43 (4H, m); 2.09 (4H, m).

APCI-MS m/z: 343.3/345.3 [MH^+].

Example 34

6-Bromo-2-[4-(methylsulfonyl)phenyl]-3H-imidazo[4,5-b]pyridine trifluoroacetate

The title compound was prepared from 5-bromo-2,3-diaminopyridine (0.060 g, 0.32 mmol) and 4-methylsulphonylbenzaldehyde (0.055 g, 0.30 mmol).

^{1}H NMR (CD_3OD): δ 8.59 (1H, dd); 8.20 (1H, dd); 8.02 (4H, s); 3.35 (3H, s).
APCI-MS m/z: 352.0/354.0 [MH^+].

Example 35

N,N-Dimethyl-N-[4-(6-methyl-3H-imidazo[4,5-b]pyridin-2-yl)phenyl]amine bis(trifluoroacetate)

The title compound was prepared from 2,3-diamino-5-methylpyridine (0.037 g, 0.30 mmol) and 4-dimethylaminobenzaldehyde (0.045 g, 0.30 mmol).

^{1}H NMR (CD_3OD): δ 8.31 (1H, brs); 8.01 (2H, brd); 7.97 (1H, brs); 6.93 (2H, brd); 3.13 (6H, s); 2.55 (3H, s).
APCI-MS m/z: 253.1/254.2 [MH^+].

Example 36

2-(4-Isopropoxyphenyl)-6-methyl-3H-imidazo[4,5-b]pyridine trifluoroacetate

The title compound was prepared from 2,3-diamino-5-methylpyridine (0.088 g, 0.72 mmol) and 4-isopropoxybenzaldehyde (0.117 g, 0.72 mmol).

^{1}H NMR (CD_3OD): δ 8.34 (1H, brs); 8.15 (1H, brs); 8.11 (2H, dd); 7.12 (2H, dd); 4.77 (1H, m); 2.57 (3H, s); 1.38 (6H, d).

APCI-MS m/z: 268.0/269.2 [MH^+].

Example 37

6-Bromo-2-(4-nitrophenyl)-3H-imidazo[4,5-b]pyridine

The title compound was prepared from 5-bromo-2,3-diaminopyridine (0.94 g, 5 mmol) and 4-nitrobenzaldehyde (0.76 g, 5 mmol).

^{1}H NMR (DMSO-d_6): δ 8.49 (1H, d); 8.44 (4H, dd); 8.37 (1H, d).

APCI-MS m/z: 319.0/321.0 [MH^+].

Example 38

N-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenyl]acetamide trifluoroacetate

The title compound was prepared from 5-bromo-2,3-diaminopyridine (0.056 g, 0.30 mmol) and 4-acetamidobenzaldehyde (0.049 g, 0.30 mmol).

^{1}H NMR (DMSO-d_6): δ 13.64 (1H, s, NH tautomer); 13.22 (1H, s, NH tautomer); 10.23 (1H, s); 8.32 (1H, brd); 8.15 (2H, brd); 7.76 (2H, brd); 2.10 (3H, s).

APCI-MS m/z: 331.1/333.1 [MH^+].

Example 39

6-Bromo-2-[4-(morpholin-4-ylmethyl)phenyl]-3*H*-imidazo[4,5-*b*]pyridine bis(trifluoroacetate)

a) 6-Bromo-2-(4-methylphenyl)-3*H*-imidazo[4,5-*b*]pyridine

The title compound was prepared from 5-bromo-2,3-diaminopyridine and 4-methylbenzaldehyde using the method described in Example 1.

^{1}H NMR (DMSO-d_6): δ 13.66 (NH-tautomer, s); 13.27 (NH-tautomer, s); 8.37 (1H, brs); 8.28 (1H, brs); 8.10 (2H, d); 7.37 (2H, d); 2.38 (3H, s).

APCI-MS m/z: 288/290 [MH^+].

b) 6-Bromo-2-[4-(bromomethyl)phenyl]-3*H*-imidazo[4,5-*b*]pyridine

The title compound was prepared by refluxing 6-bromo-2-(4-methylphenyl)-3*H*-imidazo[4,5-*b*]pyridine with a large excess of bromine in acetic acid overnight.

APCI-MS m/z: 366/368/370 [MH^+].

c) 6-Bromo-2-[4-(morpholin-4-ylmethyl)phenyl]-3*H*-imidazo[4,5-*b*]pyridine bis(trifluoroacetate)

The title compound was prepared by heating 6-bromo-2-[4-(bromomethyl)phenyl]-3*H*-imidazo[4,5-*b*]pyridine with an excess of morpholine in NMP at 60 °C for 30 minutes and was purified by RP-HPLC (10-50 % acetonitrile).

^{1}H NMR (DMSO-d_6): δ 10.37 (1H, brs); 8.90 (1H, brs); 8.44 (1H, d); 8.31 (2H, d); 7.70 (2H, d); 4.42 (2H, s); 4.02-3.60 (4H, dm); 3.34-3.07 (4H, m).

APCI-MS m/z: 373.2/375.2 [MH^+].

Example 40

6-Bromo-2-(6-morpholin-4-ylpyridin-3-yl)-3*H*-imidazo[4,5-*b*]pyridine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-(6-chloropyridin-3-yl)-3*H*-imidazo[4,5-*b*]pyridine and morpholine using the method described in Example 204.

^{1}H NMR (CD_3OD): δ 8.88 (1H, d); 8.46 (1H, d); 8.28-8.25 (1H, dd); 8.16 (1H, d); 7.05 (1H, d); 3.82 (4H, t); 3.72 (4H, t).

APCI-MS m/z: 360.1/362.0 [MH^+].

Example 41

2-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]acetamide

To a mixture of 4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenol (58 mg, 0.2 mmol) and sodium hydride (55-65%, 18 mg, 0.4 mmol) in DMF (6 ml), 2-chloroacetamide (19 mg, 0.2 mmol) was added and the mixture was heated to 60 °C for 1 h. Column chromatography on silica using ethyl acetate/methanol as eluent afforded the title compound.

^{1}H NMR (DMSO-d_6): δ 13.61 (1H, brs); 8.36 (1H, brs); 8.21 (1H, brs); 8.16 (2H, d); 7.58 (1H, brs); 7.42 (1H, brs); 7.13 (2H, d); 4.53 (2H, s).

APCI-MS m/z: 347/349 [MH^+].

Example 42

Ethyl [4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]acetate

The title compound was prepared from 4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenol and ethyl chloroacetate using the method described in Example 41.

^{1}H NMR (DMSO-d_6): δ 13.48 (1H, brs); 8.36 (1H, d); 8.21 (1H, brs); 8.15 (2H, d); 7.12 (2H, d); 4.89 (2H, s); 4.18 (2H, q); 1.21 (3H, t).

APCI-MS m/z: 376/378 [MH^+].

Example 43

N-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-methylamine

The title compound was prepared from 4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenol and *tert*-butyl 2-bromoethyl(methyl)carbamate using the method described in Example 41, followed by deprotection using trifluoroacetic acid.

^{1}H NMR (DMSO-d_6): δ 8.35 (1H, s); 8.19 (1H, s); 8.15 (2H, d); 7.12 (2H, d); 4.11 (2H, t); 3.31 (2H (NH), brs); 2.87 (2H, t); 2.35 (3H, s).

APCI-MS m/z: 347/349 [MH^+].

Example 44

6-Bromo-2-[4-(3-chloropropoxy)phenyl]-3H-imidazo[4,5-b]pyridine

The title compound was prepared from 4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenol and 1-bromo-3-chloropropane using the method described in Example 41.

^{1}H NMR (DMSO-d_6): δ 13.58 (1H, brs); 8.35 (1H, brs); 8.22 (1H, brs); 8.15 (2H, d); 7.14 (2H, d); 4.18 (2H, t); 3.80 (2H, t); 2.19 (2H, qv).

APCI-MS m/z: 365.9/367.9 [MH^+].

Example 45

3-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]propan-1-amine

a) 2-{3-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]propyl}-1*H*-isoindole-1,3(2*H*)-dione

The title compound was prepared from 4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenol and 2-(3-bromopropyl)-1*H*-isoindole-1,3(2*H*)-dione using the method described in Example 41.

^{1}H NMR (DMSO-d_6): δ 13.40 (1H, brs); 8.34 (1H, d); 8.17 (1H, d); 8.10 (2H, d); 7.88-7.80 (4H, m); 6.96 (2H, d); 4.11 (2H, t); 3.77 (2H, t); 2.08 (2H, qv).

APCI-MS m/z: 477/479 [MH^+].

b) 3-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]propan-1-amine

The title compound was prepared by stirring 2-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]propyl}-1*H*-isoindole-1,3(2*H*)-dione with a large excess of methylamine in ethanol for two days and was purified by column chromatography on silica.

^{1}H NMR (DMSO-d_6): δ 8.30 (1H, d); 8.15 (2H, d); 8.13 (1H, d); 7.09 (2H, d); 5.76 (2H, brs); 4.12 (2H, (NH2), t); 3.42 (1H, (NH), brs); 2.73 (2H, t); 1.83 (2H, qv).

APCI-MS m/z: 347/349 [MH^+].

Example 46

6-Bromo-2-[4-(3-morpholin-4-ylpropoxy)phenyl]-3H-imidazo[4,5-b]pyridine

A solution of 6-bromo-2-[4-(3-chloropropoxy)phenyl]-3H-imidazo[4,5-b]pyridine (50 mg, 0.14 mmol), lithium iodide (20 mg, 0.15 mmol) and morpholine (0.1 ml, 1.15 mmol) in DMF (5 ml) was heated at 100 °C for 6 h. Column chromatography on silica using methylene chloride/methanol/ammonia as eluent afforded the title compound in almost quantitative yield.

^{1}H NMR (DMSO-d_6): δ 13.10 (1H, brs); 8.34 (1H, d); 8.17 (1H, d); 8.14 (2H, d); 7.11 (2H, d); 4.10 (2H, t); 3.56 (4H, t); 2.42 (2H, t); 2.36 (4H, brm); 1.89 (2H, qv).

APCI-MS m/z: 417/419 [MH^+].

Example 47

6-Bromo-2-[4-(3-piperidin-1-ylpropoxy)phenyl]-3H-imidazo[4,5-b]pyridine

The title compound was prepared from 6-bromo-2-[4-(3-chloropropoxy)phenyl]-3H-imidazo[4,5-b]pyridine and piperidine using the method described in Example 46.

^{1}H NMR (DMSO-d_6): δ 13.45 (1H, brs); 8.35 (1H, d); 8.18 (1H, brs); 8.14 (2H, d); 7.11 (2H, d); 4.08 (2H, t); 2.38 (2H, t); 2.32 (4H, brm); 1.87 (2H, qv); 1.48 (4H, qv); 1.37 (2H, m).

APCI-MS m/z: 415.1/417.1 [MH^+].

Example 48

6-Bromo-2-[4-(3-pyrrolidin-1-ylpropoxy)phenyl]-3H-imidazo[4,5-b]pyridine

The title compound was prepared from 6-bromo-2-[4-(3-chloropropoxy)phenyl]-3H-imidazo[4,5-b]pyridine and pyrrolidine using the method described in Example 46.

^{1}H NMR (DMSO-d_6): δ 13.22 (1H, brs); 8.35 (1H, d); 8.19 (1H, brs); 8.15 (2H, d); 7.11 (2H, d); 4.11 (2H, t); 2.61 (2H, t); 2.53 (4H, m); 1.93 (2H, qv); 1.70 (4H, m).

APCI-MS m/z: 401.1/403.1 [MH^+].

Example 49

6-Bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine

2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethanol (2.0 g, 6 mmol) was dissolved and refluxed in thionyl chloride (30 ml) for 3 h. The excess thionyl chloride was evaporated off and the residue was co-evaporated twice with toluene affording the title product in quantitative yield.

^{1}H NMR (DMSO-d_6): δ 13.60 (NH-tautomer, s); 13.20 (NH-tautomer, s); 8.34 (1H, d); 8.25 (1H, brs); 8.16 (2H, d); 7.15 (2H, d); 4.35 (2H, t); 3.97 (2H, t).

APCI-MS m/z: 351.9/353.9 [MH^+].

Example 50

6-Bromo-2-[4-(2-morpholin-4-ylethoxy)phenyl]-3H-imidazo[4,5-b]pyridine

A solution of 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine (50 mg, 0.14 mmol), morpholine (0.037 ml, 0.42 mmol) in NMP (5 ml) and N-ethyldiisopropylamine (0.24 ml, 1.4 mmol) was heated at 120 °C for 6 h. Column chromatography on silica using methylene chloride/methanol/ammonia as eluent afforded the title compound.

^{1}H NMR (DMSO-d_6): δ 13.58 (NH-tautomer, brs); 13.18 (NH-tautomer, brs); 8.33 (1H, m); 8.25 (1H, m); 8.15 (2H, m); 7.13 (2H, m); 4.18 (2H, t); 3.57 (4H, m); 2.72 (2H, m); 2.49 (4H, m).

APCI-MS m/z: 403/405 [MH^+].

Using the general method of Example 50, the compounds of Examples 51 to 119 were prepared:

Example 51

N-{2-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]ethyl}-*N*-(tetrahydrofuran-2-ylmethyl)amine

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and tetrahydrofurfurylamine.

^{1}H NMR (DMSO-d_6): δ 13.30 (1H, brs); 8.36 (1H, s); 8.22 (1H, brs); 8.15 (2H, d); 7.13 (2H, d); 4.13 (2H, t); 3.88 (1H, m); 3.73 (1H, m); 3.60 (1H, m); 2.95 (2H, t); 2.65 (2H, m); 1.89 (1H, m); 1.79 (2H, m); 1.51 (1H, m).

APCI-MS m/z: 417.1/419.1 [MH^+].

Example 52

6-Bromo-2-[4-(2-pyrrolidin-1-ylethoxy)phenyl]-3H-imidazo[4,5-b]pyridine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and pyrrolidine.

APCI-MS m/z: 387.4/389.4 [MH^+].

Example 53

2-[{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}(methyl)amino]ethanol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 2-(methylamino)ethanol.

APCI-MS m/z: 391.4/393.4 [MH^+].

Example 54

3-[{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}(methyl)amino]propanenitrile bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 3-(methylamino)propanenitrile.

APCI-MS m/z: 400.3/402.4 [MH^+].

Example 55

6-Bromo-2-[4-(2-morpholin-4-ylethoxy)phenyl]-3H-imidazo[4,5-b]pyridine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and morpholine.

APCI-MS m/z: 403.4/405.4 [MH^+].

Example 56

1-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}pyrrolidin-3-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and pyrrolidin-3-ol.

APCI-MS m/z: 403.4/405.4 [MH^+].

Example 57

6-Bromo-2-{4-[2-(4-methylpiperazin-1-yl)ethoxy]phenyl}-3H-imidazo[4,5-b]pyridine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 1-methylpiperazine.

APCI-MS m/z: 416.4/418.4 [MH^+].

Example 58

1-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N,N-dimethylpyrrolidin-3-amine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and *N*,*N*-dimethylpyrrolidin-3-amine.

APCI-MS m/z: 430.4/432.4 [MH^+].

Example 59

N-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N,1-dimethylpyrrolidin-3-amine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and *N*,1-dimethylpyrrolidin-3-amine.

APCI-MS m/z: 430.4/432.4 [MH^+]

Example 60

N^2-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N^1,N^1,N^2-trimethylglycinamide bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and N^1,N^1,N^2-trimethylglycinamide.

APCI-MS m/z: 432.4/434.4 [MH^+].

Example 61

N-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-ethyl-N',N'-dimethylethane-1,2-diamine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and *N'*-ethyl-*N*,*N*-dimethylethane-1,2-diamine.

APCI-MS m/z: 432.4/434.4 [MH^+].

Example 62

N-Benzyl-N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-methylamine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and *N*-benzyl-*N*-methylamine.

APCI-MS m/z: 437.4/439.4 [MH^+].

Example 63

2-{4-[2-(4-Acetylpiperazin-1-yl)ethoxy]phenyl}-6-bromo-3H-imidazo[4,5-b]pyridine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 1-acetylpiperazine.

APCI-MS m/z: 444.4/446.4 [MH^+].

Example 64

N-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N,N-bis(2-methoxyethyl)amine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and *N*,*N*-bis(2-methoxyethyl)amine.

APCI-MS m/z: 449.5/451.5 [MH^+].

Example 65

N-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-methyl-N-(2-phenylethyl)amine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and *N*-methyl-*N*-(2-phenylethyl)amine.

APCI-MS m/z: 451.5/453.4 [MH^+].

Example 66

6-Bromo-2-{4-[2-(4-phenylpiperazin-1-yl)ethoxy]phenyl}-3H-imidazo[4,5-b]pyridine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 1-phenylpiperazine.

APCI-MS m/z: 478.5/480.5 [MH^+].

Example 67

6-Bromo-2-{4-[2-(4-pyridin-2-ylpiperazin-1-yl)ethoxy]phenyl}-3H-imidazo[4,5-b]pyridine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 1-pyridin-2-ylpiperazine.

APCI-MS m/z: 479.4/481.4 [MH^+].

Example 68

N-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-[3-(1H-imidazol-1-yl)propyl]amine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 3-(1*H*-imidazol-1-yl)propan-1-amine.

APCI-MS m/z: 441.4/443.4 [MH^+].

Example 69

N-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(4-methoxybenzyl)amine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 4-methoxybenzylamine.

APCI-MS m/z: 453.4/455.5 [MH^+].

Example 70

N-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(3-methoxybenzyl)amine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 3-methoxybenzylamine.

APCI-MS m/z: 453.4/455.5 [MH^+].

Example 71

N-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(4-chlorobenzyl)amine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 4-chlorobenzylamine.

APCI-MS m/z: 457.4/459.4 [MH^+].

Example 72

N-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(3-chlorobenzyl)amine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 3-chlorobenzylamine.

APCI-MS m/z: 457.3/459.4 [MH^+].

Example 73

Ethyl 4-({2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}amino)piperidine-1-carboxylate bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and ethyl 4-aminopiperidine-1-carboxylate.

APCI-MS m/z: 488.5/490.5 [MH^+].

Example 74

6-Bromo-2-(4-{2-[4-(2-methoxyethyl)piperazin-1-yl]ethoxy}phenyl)-3H-imidazo[4,5-b]pyridine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 1-(2-methoxyethyl)piperazine.

APCI-MS m/z: 460.5/462.5 [MH^+].

Example 75

1-({2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}amino)propan-2-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 1-amino-2-propanol.

APCI-MS m/z: 391.4/393.4 [MH^+].

Example 76

N-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(2-methoxyethyl)amine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 2-methoxyethylamine.

APCI-MS m/z: 391.4/393.3 [MH^+].

Example 77

2-({2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}amino)propan-1-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and DL-2-aminopropan-1-ol.

APCI-MS m/z: 391.4/393.3 [MH^+].

Example 78

N-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(2-furylmethyl)amine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and furfurylamine.

APCI-MS m/z: 413.4/415.4 [MH^+].

Example 79

N-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(tetrahydrofuran-2-ylmethyl)amine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and tetrahydrofurfurylamine.

APCI-MS m/z: 417.4/419.4 [MH^+].

Example 80

N-Benzyl-N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}amine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and benzylamine.

APCI-MS m/z: 423.4/425.4 [MH^+].

Example 81

N-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(pyridin-3-ylmethyl)amine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 1-pyridin-3-ylmethanamine.

APCI-MS m/z: 424.4/426.4 [MH^+].

Example 82

N-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(pyridin-4-ylmethyl)amine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 1-pyridin-4-ylmethanamine.

APCI-MS m/z: 424.4/426.4 [MH^+].

Example 83

N-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(thien-2-ylmethyl)amine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 1-thien-2-ylmethanamine.

APCI-MS m/z: 429.3/431.3 [MH^+].

Example 84

N-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(1-phenylethyl)amine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and D,L-1-phenylethylamine.

APCI-MS m/z: 437.4/439.4 [MH^+].

Example 85

N-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-1-ethylpiperidin-3-amine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 1-ethylpiperidin-3-amine.

APCI-MS m/z: 444.5/446.5 [MH^+].

Example 86

N-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(2-morpholin-4-ylethyl)amine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 2-morpholin-4-ylethanamine.

APCI-MS m/z: 446.4/448.4 [MH^+].

Example 87

N-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(2-methoxybenzyl)amine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 2-methoxybenzylamine.

APCI-MS m/z: 453.4/455.4 [MH^+].

Example 88

1-[3-({2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}amino)propyl]pyrrolidin-2-one bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 1-(3-aminopropyl)pyrrolidin-2-one.

APCI-MS m/z: 458.5/460.4 [MH^+].

Example 89

N-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-[2-(4-chlorophenyl)ethyl]amine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 2-(4-chlorophenyl)ethanamine.

APCI-MS m/z: 471.4/473.4 [MH^+].

Example 90

4-[{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}(methyl)amino]cyclohexanecarbonitrile bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 4-(methylamino)cyclohexanecarbonitrile.

APCI-MS m/z: 454.4/456.4 [MH^+].

Example 91

1-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperidin-3-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and piperidin-3-ol.

APCI-MS m/z: 417.4/419.4 [MH^+].

Example 92

6-Bromo-2-{4-[2-(2-pyridin-3-ylpiperidin-1-yl)ethoxy]phenyl}-3H-imidazo[4,5-b]pyridine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 3-piperidin-2-ylpyridine.

APCI-MS m/z: 478.4/480.5 [MH^+].

Example 93

N-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-cyclopentylamine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and cyclopentylamine.

APCI-MS m/z: 401.4/403.4 [MH^+].

Example 94

1-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-4-phenylpiperidin-4-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 4-phenylpiperidin-4-ol.

APCI-MS m/z: 493.5/495.5 [MH^+].

Example 95

N-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-[2-(1H-imidazol-4-yl)ethyl]amine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 2-(1*H*-imidazol-4-yl)ethanamine dihydrochloride.

APCI-MS m/z: 427.4/429.4 [MH^+].

Example 96

1-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperidine-3-carboxamide bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and piperidine-3-carboxamide.

APCI-MS m/z: 444.4/446.4 [MH^+].

Example 97

6-Bromo-2-{4-[2-(4-pyrazin-2-ylpiperazin-1-yl)ethoxy]phenyl}-3H-imidazo[4,5-b]pyridine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 2-piperazin-1-ylpyrazine.

APCI-MS m/z: 480.5/482.4 [MH^+].

Example 98

(1*S*,2*S*)-2-({2-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]ethyl}amino)cyclohexanol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and (1*S*,2*S*)-2-aminocyclohexanol hydrochloride.

APCI-MS m/z: 431.4/433.4 [MH^+].

Example 99

6-Bromo-2-(4-{2-[4-(3-methoxyphenyl)piperazin-1-yl]ethoxy}phenyl)-3H-imidazo[4,5-b]pyridine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 1-(3-methoxyphenyl)piperazine.

APCI-MS m/z: 508.5/510.5 [MH^+].

Example 100

(1-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperidin-4-yl)methanol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and piperidin-4-ylmethanol.

APCI-MS m/z: 431.4/433.4 [MH^+].

Example 101

4-({2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}amino)cyclohexanol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 4-aminocyclohexanol hydrochloride.

APCI-MS m/z: 431.4/433.4 [MH^+].

Example 102

(1-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperidin-2-yl)methanol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and piperidin-2-ylmethanol.

APCI-MS m/z: 431.4/433.4 [MH^+].

Example 103

1'-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-1,4'-bipiperidine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 1,4'-bipiperidine.

APCI-MS m/z: 484.5/486.5 [MH^+].

Example 104

N-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-1,3-thiazol-2-amine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 2-aminothiazole.

APCI-MS m/z: 416.3/418.3 [MH^+].

Example 105

1-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperidine-4-carboxamide bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and piperidine-4-carboxamide.

APCI-MS m/z: 444.4/446.4 [MH^+].

Example 106

N-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-1H-1,2,4-triazol-3-amine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 1*H*-1,2,4-triazol-3-amine.

APCI-MS m/z: 400.3/402.3 [MH^+].

Example 107

2-(4-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperazin-1-yl)benzonitrile bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 2-piperazin-1-ylbenzonitrile.

APCI-MS m/z: 503.5/505.5 [MH^+].

Example 108

6-(4-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperazin-1-yl)nicotinonitrile bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 6-piperazin-1-ylnicotinonitrile.

APCI-MS m/z: 504.5/506.5 [MH^+].

Example 109

1-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}prolinamide bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and D-prolinamide.

APCI-MS m/z: 430.4/432.4 [MH^+].

Example 110

6-Bromo-2-(4-{2-[4-(2-methoxyphenyl)piperidin-1-yl]ethoxy}phenyl)-3H-imidazo[4,5-b]pyridine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 4-(2-methoxyphenyl)piperidine.

APCI-MS m/z: 507.5/509.5 [MH^+].

Example 111

2-(4-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperazin-1-yl)ethanol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 2-piperazin-1-ylethanol.

APCI-MS m/z: 446.4/448.4 [MH^+].

Example 112

1-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperidin-4-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and piperidin-4-ol.

APCI-MS m/z: 417.4/419.4 [MH^+].

Example 113

6-Bromo-2-(4-{2-[4-(2-methoxyphenyl)piperazin-1-yl]ethoxy}phenyl)-3H-imidazo[4,5-b]pyridine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 1-(2-methoxyphenyl)piperazine.

APCI-MS m/z: 508.5/510.5 [MH^+].

Example 114

(2*S*)-2-({2-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]ethyl}amino)-3-methylbutan-1-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and (2*S*)-2-amino-3-methylbutan-1-ol.

APCI-MS m/z: 419.4/421.4 [MH^+].

Example 115

N-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-4,5-dihydro-1,3-thiazol-2-amine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 4,5-dihydro-1,3-thiazol-2-amine.

APCI-MS m/z: 418.3/420.3 [MH^+].

Example 116

N-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-[2-(1H-indol-3-yl)ethyl]amine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 2-(1*H*-indol-3-yl)ethanamine.

APCI-MS m/z: 476.4/478.4[MH^+].

Example 117

(2*S*)-2-({2-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]ethyl}amino)-2-phenylethanol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and (2*R*)-2-amino-2-phenylethanol.

APCI-MS m/z: 453.4/455.4 [MH^+].

Example 118

N-{2-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-1H-tetrazol-5-amine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 1*H*-tetrazol-5-amine.

APCI-MS m/z: 401.3/403.4 [MH^+].

Example 119

(1*S*,2*R*)-2-({2-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]ethyl}amino)cyclohexanol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(2-chloroethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and (1*R*,2*S*)-2-aminocyclohexanol hydrochloride.

APCI-MS m/z: 431.4/433.4 [MH^+].

Example 120

6-Methoxy-2-(4-methoxyphenyl)-3H-imidazo[4,5-b]pyridine trifluoroacetate

Sodium methoxide, obtained from methanol (4 ml) and sodium (1.23 g, 53 mmol) was added to a solution of 6-bromo-2-(4-methoxyphenyl)-3H-imidazo[4,5-b]pyridine (0.304 g, 1 mmol) and cuprous bromide (0.286 g, 2 mmol) in DMF (6.4 ml). The reaction mixture was heated under reflux overnight. After cooling, water (100 ml) was added and the precipitate was filtered off. The solid substance was dissolved in DMF (5 ml) and purified by RP-HPLC (10-60 % acetonitrile) to give the title compound.

^{1}H NMR (DMSO-d_6): δ 8.15 (3H, d); 7.62 (1H, s); 7.16 (2H, d); 3.90 (3H, s); 3.86 (3H, s).

APCI-MS m/z: 256.2 [MH^+].

Example 121

6-Bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine

4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenol (2 g, 6.89 mmol) was dissolved in DMF (200 ml) and sodium hydride (0.9 g, 20.67 mmol, 55% in oil) was added. The mixture was stirred at 50 °C for 1 h, and epibromohydrin (0.94 ml, 11.37 mmol) was added dropwise followed by stirring for one h at room temperature. Purification by flash chromatography on silica using ethyl acetate/heptane as eluent afforded the title compound (0.55 g, 23 %).

APCI-MS m/z: 346/348 [MH^+].

^{1}H NMR (DMSO-d_6): δ 8.37 (1H, d); 8.20 (1H, brs); 8.17 (2H, d); 7.16 (2H, d); 4.47-4.43 (1H, dd); 3.96-3.92 (1H, dd); 2.87 (1H, t); 2.75-2.73 (1H, dd).

Example 122

1-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-pyrrolidin-1-ylpropan-2-ol

To a solution of 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine (119 mg, 0.35 mmol) in DMF (8 ml), pyrrolidine (144 µl, 1.73 mmol) was added. The mixture was heated at 85 °C for 10 h. 5 % Aqueous ammonium chloride was added and the mixture was extracted with ethyl acetate. The organic phase was filtered and concentrated. Purification by flash chromatography on silica using methylene chloride/methanol/ammonia as eluent afforded the title compound (35 mg, 24%).

^{1}H NMR (CD_3OD): δ 8.37 (1H, s); 8.10-8.07 (3H, m); 7.14 (2H, d); 4.19-4.10 (2H, m); 4.06-4.02 (1H, m); 2.86-2.82 (1H, m); 2.74-2.69 (5H, m); 1.88-1.82 (4H, m).

APCI-MS m/z: 417/419 [MH^+].

Using the general method of Example 122, the compounds of Examples 123 to 173 were prepared:

Example 123

1-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-morpholin-4-ylpropan-2-ol

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and morpholine.

^{1}H NMR (CD_3OD): δ 8.37 (1H, d); 8.09-8.06 (3H, m); 7.14 (2H, d); 4.18-4.11 (2H, m); 4.07-4.02 (1H, m); 3.71 (4H, t); 2.59-2.55 (6H, m).

APCI-MS m/z: 433/435 [MH^+].

Example 124

1-{3-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}pyrrolidin-3-ol

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and pyrrolidin-3-ol.

^{1}H NMR (CD_3OD): δ 8.38 (1H, d); 8.10-8.07 (3H, m); 7.15 (2H, d); 4.48-4.42 (1H, m); 4.27-4.18 (1H, m); 4.15-4.05 (2H, m); 3.27-2.93 (6H, m); 2.27-2.15 (1H, m); 1.92-1.85 (1H, m).

APCI-MS m/z: 433/435 [MH^+].

Example 125

1-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-piperidin-1-ylpropan-2-ol

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and piperidine.

^{1}H NMR (CD_3OD): δ 8.39 (1H, d); 8.10-8.08 (3H, m); 7.15 (2H, d); 4.23-4.19 (1H, m); 4.13-4.10 (1H, m); 4.06-4.02 (1H, m); 2.74-2.65 (6H, m); 1.69-1.65 (4H, m); 1.55-1.51 (2H, m).

APCI-MS m/z: 431/433 [MH^+].

Example 126

1-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-(diethylamino)propan-2-ol

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and diethylamine.

^{1}H NMR (CD_3OD): δ 8.38 (1H, d); 8.10-8.07 (3H, m); 7.15 (2H, d); 4.15-4.05 (3H, m); 2.85-2.70 (6H, m); 1.13 (6H, t).

APCI-MS m/z: 419/421 [MH^+].

Example 127

1-{3-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}piperidin-4-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and piperidin-4-ol.

^{1}H NMR (CD_3OD): δ 8.50 (1H, d); 8.21 (1H, d); 8.13 (2H, d); 7.22 (2H, d); 4.50-4.42 (1H, m); 4.17-4.11 (3H, m); 3.91-3.83 (1H, m); 3.75-3.69 (1H, m); 3.54-3.08 (5H, m); 2,20-1.75 (4H, m).

APCI-MS m/z: 447/449 [MH^+].

Example 128

1-(4-Acetylpiperazin-1-yl)-3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]propan-2-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine (10 mg, 0.03 mmol) and 1-acetylpiperazine (37 mg, 0.29 mmol). Purification by preparative HPLC gave the required compound (8 mg, 39 %).

^{1}H NMR (CD_3OD): δ 8.50 (1H, d); 8.21 (1H, d); 8.13 (2H, d); 7.21 (2H, d); 4.53-4.47 (1H, m); 4.19-4.13 (2H, m); 4,01-3.89 (2H, m); 3.64-3.33 (6H, m); 2.17 (3H, s).

APCI-MS m/z: 474/476 [MH^+].

Example 129

1-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[3-(dimethylamino)pyrrolidin-1-yl]propan-2-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine (10 mg, 0.03 mmol) and 3-dimethylaminepyrrolidine (13 mg, 0.12 mmol).

^{1}H NMR (CD_3OD): δ 8.49 (1H, d); 8.20 (1H, d); 8.13 (2H, d); 7.21 (2H, d); 4.44-4.38 (1H, m); 4.23-4.13 (3H, m); 4.04-3.97 (1H, m); 3.93-3.89 (1H, m); 3.79 (1H, brs); 3.62-3.53 (3H, m); 2.99 (6H, s); 2.70-2.61 (1H, m); 2.47-2.38 (1H, m).

APCI-MS m/z: 460/462 [MH^+].

Example 130

4-[({2-Hydroxy-3-[4-(6-methyl-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]propyl}amino)methyl]phenol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine (15 mg, 0.04 mmol) and 4-methoxybenzylamine (28 µl, 0.22 mmol).

APCI-MS m/z: 483/485 [MH^+].

Example 131

1-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(2-hydroxyethyl)(methyl)amino]propan-2-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 2-(methylamino)ethanol.

APCI-MS m/z: 421/423 [MH^+].

Example 132

3-[{3-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}(methyl)amino]propanenitrile bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 3-(methylamino)propanenitrile.

APCI-MS m/z: 430/432 [MH^+].

Example 133

4-{3-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}piperazin-1-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 1-methylpiperazine.

APCI-MS m/z: 446/448 [MH^+].

Example 134

N^2-{3-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}-N^1,N^1,N^2-trimethylglycinamide bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and N^1,N^1,N^2-trimethylglycinamide.

APCI-MS m/z: 462/464 [MH^+].

Example 135

1-[Benzyl(methyl)amino]-3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]propan-2-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and *N*-benzyl-*N*-methylamine.

APCI-MS m/z: 467/469 [MH^+].

Example 136

1-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[methyl(2-phenylethyl)amino]propan-2-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and *N*-methyl-*N*-(2-phenylethyl)amine.

APCI-MS m/z: 481/483 [MH^+].

Example 137

1-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-(4-phenylpiperazin-1-yl)propan-2-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 1-phenylpiperazine.

APCI-MS m/z: 508/510 [MH^+].

Example 138

1-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-(4-pyridin-2-ylpiperazin-1-yl)propan-2-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 1-pyridin-2-ylpiperazine.

APCI-MS m/z: 509/511 [MH^+].

Example 139

1-[2-({3-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}amino)ethyl]imidazolidin-2-one bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 1-(2-aminoethyl)imidazolidin-2-one.

APCI-MS m/z: 475/477 [MH^+].

Example 140

1-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(3-methoxybenzyl)amino]propan-2-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 3-methoxybenzylamine.

APCI-MS m/z: 483/485 [MH^+].

Example 141

1-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(2-chlorobenzyl)amino]propan-2-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 2-chlorobenzylamine.

APCI-MS m/z: 487/489 [MH^+].

Example 142

1-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(4-chlorobenzyl)amino]propan-2-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 4-chlorobenzylamine.

APCI-MS m/z: 487/489 [MH^+].

Example 143

1-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(3-chlorobenzyl)amino]propan-2-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 3-chlorobenzylamine.

APCI-MS m/z: 487/489 [MH^+].

Example 144

Ethyl 4-({3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}amino)piperidine-1-carboxylate bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and ethyl 4-aminopiperidine-1-carboxylate.

APCI-MS m/z: 518/520 [MH^+].

Example 145

1-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[4-(2-methoxyethyl)piperazin-1-yl]propan-2-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 1-(2-methoxyethyl)piperazine.

APCI-MS m/z: 490/492 [MH^+].

Example 146

1-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-(cyclopropylamino)propan-2-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and cyclopropylamine.

APCI-MS m/z: 403/405 [MH^+].

Example 147

3-({3-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}amino)propan-2-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 1-amino-2-propanol.

APCI-MS m/z: 421/423 [MH^+].

Example 148

1-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(2-methoxyethyl)amino]propan-2-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 2-methoxyethylamine.

APCI-MS m/z: 421/423 [MH^+].

Example 149

2-({3-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}amino)propan-1-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and DL-2-aminopropan-1-ol.

APCI-MS m/z: 421/423 [MH^+].

Example 150

1-(Benzylamino)-3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]propan-2-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and benzylamine.

APCI-MS m/z: 453/455 [MH^+].

Example 151

1-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(pyridin-3-ylmethyl)amino]propan-2-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 1-pyridin-3-ylmethanamine.

APCI-MS m/z: 454/456 [MH^+].

Example 152

1-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(pyridin-4-ylmethyl)amino]propan-2-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 1-pyridin-4-ylmethanamine.

APCI-MS m/z: 454/456 [MH^+].

Example 153

1-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(1-ethylpiperidin-3-yl)amino]propan-2-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 1-ethylpiperidin-3-amine.

APCI-MS m/z: 474/476 [MH^+].

Example 154

1-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(2-morpholin-4-ylethyl)amino]propan-2-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 2-morpholin-4-ylethanamine.

APCI-MS m/z: 476/478 [MH^+].

Example 155

1-[3-({3-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}amino)propyl]pyrrolidin-2-one bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 1-(3-aminopropyl)pyrrolidin-2-one.

APCI-MS m/z: 488/490 [MH^+].

Example 156

1-{3-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}piperidin-3-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and piperidin-3-ol.

APCI-MS m/z: 447/449 [MH^+].

Example 157

1-{3-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}prolinamide bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and D-prolinamide.

APCI-MS m/z: 460/462 [MH^+].

Example 158

1-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[4-(hydroxymethyl)piperidin-1-yl]propan-2-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and piperidin-4-ylmethanol.

APCI-MS m/z: 461/463 [MH^+].

Example 159

1-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[2-(hydroxymethyl)piperidin-1-yl]propan-2-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and piperidin-2-ylmethanol.

APCI-MS m/z: 461/463 [MH^+].

Example 160

1-{3-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}piperidine-4-carboxamide bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and piperidine-4-carboxamide.

APCI-MS m/z: 474/476 [MH^+].

Example 161

1-{3-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}piperidine-3-carboxamide bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and piperidine-3-carboxamide.

APCI-MS m/z: 474/476 [MH^+].

Example 162

1-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[4-(2-hydroxyethyl)piperazin-1-yl]propan-2-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 2-piperazin-1-ylethanol.

APCI-MS m/z: 476/478 [MH^+].

Example 163

2-(4-{3-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}piperazin-1-yl)benzonitrile bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 2-piperazin-1-ylbenzonitrile.

APCI-MS m/z: 533/535 [MH^+].

Example 164

6-(4-{3-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}piperazin-1-yl)nicotinonitrile bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 6-piperazin-1-ylnicotinonitrile.

APCI-MS m/z: 534/536 [MH^+].

Example 165

1-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-chloropropan-2-ol trifluoroacetate

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine.

APCI-MS m/z: 382/384 [MH^+].

Example 166

1-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-(1,3-thiazol-2-ylamino)propan-2-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 2-aminothiazole.

APCI-MS m/z: 452/454 [MH^+].

Example 167

1-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-(4-pyrazin-2-ylpiperazin-1-yl)propan-2-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 2-piperazin-1-ylpyrazine.

APCI-MS m/z: 510/512 [MH^+].

Example 168

1-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(2-methoxybenzyl)amino]propan-2-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 2-methoxybenzylamine.

APCI-MS m/z: 483/485 [MH^+].

Example 169

4-[{3-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}(methyl)amino]cyclohexanecarbonitrile bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 4-(methylamino)cyclohexanecarbonitrile.

APCI-MS m/z: 484/486 [MH^+].

Example 170

1-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-(2-pyridin-3-ylpiperidin-1-yl)propan-2-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 3-piperidin-2-ylpyridine.

APCI-MS m/z: 508/510 [MH^+].

Example 171

1-{3-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}-4-phenylpiperidin-4-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 4-phenylpiperidin-4-ol.

APCI-MS m/z: 523/525 [MH^+].

Example 172

2-({3-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}amino)-3-methylbutan-1-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and (2*S*)-2-amino-3-methylbutan-1-ol.

APCI-MS m/z: 449/451 [MH^+].

Example 173

1-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[4-(3-methoxyphenyl)piperazin-1-yl]propan-2-ol bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-[4-(oxiran-2-ylmethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine and 1-(3-methoxyphenyl)piperazine.

APCI-MS m/z: 538/540 [MH^+].

Example 174

4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline

To a stirred solution of 6-bromo-2-(4-nitrophenyl)-3H-imidazo[4,5-b]pyridine (1.6 g, 5 mmol) in methanol (45 ml) ammonium sulfide (8.5 ml, 25 mmol, 20% solution in water) was added slowly. The mixture was stirred at room temperature for 30 minutes and then heated and refluxed for 5 h. The reaction mixture was concentrated and cooled to 0 °C. The precipitate was filtered off, washed with cold methanol and dried to give the title compound.

^{1}H NMR (CD_3OD): δ 7.51 (1H, brs); 7.20 (1H, brs); 7.06 (2H, dd); 5.98 (2H, dd).

APCI-MS m/z: 289.0/291.0 [MH^+].

Example 175

4-({[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]amino}methyl)benzonitrile bis(trifluoroacetate)

4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)aniline (50 mg, 0.17 mmol), 4-cyanobenzaldehyde (23 mg, 0.17 mmol) and acetic acid (50µl) were mixed in NMP (500 µl). Trimethylsilylchloride (44 µl, 0.35 mmol) and $NaBH(OAc)_3$ (73 mg, 0.35 mmol) were added and the mixture was stirred for 2 h until analytical LC-MS indicated that the reaction was complete. 1M sodium hydroxide (1 ml) was added and a precipitate was formed upon the subsequent addition of water. The precipitate was collected, washed with ice-cold ethanol and purified by preparative HPLC to yield the title product (28 mg, 26 %).

^{1}H NMR (DMSO-d_6): δ 8.33 (1H, d); 8.13 (1H, d); 7.93 (2H, d); 7.81 (2H, d); 7.55 (2H, d); 6.71 (2H, d); 4.50 (2H, s).
APCI-MS m/z: 404/406 [MH^+].

Using the general method of Example 175, the compounds of Examples 176 to 203 were prepared:

Example 176

N-Benzyl-N-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenyl]amine

The title compound was prepared from 4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline (0.289 g, 1 mmol) and benzaldehyde (0.106 g, 1 mmol).

^{1}H NMR (CD_3OD): δ 8.27 (1H, s, NH tautomer); 8.07 (1H, s, NH tautomer); 7.92 (2H, dd); 7.39-7.31 (4H, m); 7.25 (1H, brt); 6.96 (1H, t); 6.71 (2H, d); 4.37 (2H, d).
APCI-MS m/z: 379.0/381.1 [MH^+].

Example 177

N-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenyl]-N-(1H-imidazol-2-ylmethyl)amine bis(trifluoroacetate)

The title compound was prepared from 4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline (0.145 g, 0.5 mmol) and 2-imidazole carboxaldehyde (0.048 g, 0.5 mmol).

^{1}H NMR (DMSO-d_6): δ 9,75 (1H, brs); 8.38 (1H, d); 8.21 (1H, brs); 8.17 (2H, brd); 7.66 (2H, s); 7.37 (2H, brd); 4.87 (2H, brs).

APCI-MS m/z: 369.1/371.1 [MH^+].

Example 178

N-[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenyl]-N-(1H-imidazol-5-ylmethyl)amine bis(trifluoroacetate)

The title compound was prepared from 4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline (0.145 g, 0.5 mmol) and 4-formylimidazol (0.048 g, 0.5 mmol).

^{1}H NMR (CD_3OD): δ 8.87 (1H, brs); 8.47 (1H, brs); 8.15 (1H, brs); 7.96 (2H, d); 7.52 (1H, brs); 6.88 (2H, d); 4.58 (2H, s).

APCI-MS m/z: 369.0/371.0 [MH^+].

Example 179

3-({[4-(6-Bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenyl]amino}methyl)benzonitrile bis(trifluoroacetate).

The title compound was prepared from 4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline and 3-cyanobenzaldehyde.

^{1}H NMR (CD_3OD): δ 8.43 (1H, d); 8.10 (1H, d); 7.90 (2H, brd); 7.73-7.70 (2H, brm); 7.63 (1H, brd); 7.53 (1H, t); 4.53 (2H, s).

APCI-MS m/z: 404.2/406.2 [MH^+].

Example 180

N-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(4-methoxybenzyl)amine bis(trifluoroacetate)

The title compound was prepared from 4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline and 4-methoxybenzaldehyde.

^{1}H NMR (CD_3OD): δ 8.46 (1H, d); 8.12 (1H, d); 7.88 (2H, d); 7.29 (2H, d); 6.89 (2H, d); 6.80 (2H, d); 4.38 (2H, s); 3.78 (3H, s).

APCI-MS m/z: 409/411 [MH^+].

Example 181

N-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(2-methoxybenzyl)amine bis(trifluoroacetate)

The title compound was prepared from 4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline and 2-methoxybenzaldehyde.

^{1}H NMR (CD_3OD): δ 8.48 (1H, d); 8.14 (1H, d); 7.88 (2H, d); 7.28-7.23 (2H, m); 7.00 (1H, d); 6.89 (1H, t); 6.80 (2H, d); 4.44 (2H, s); 3.90 (3H, s).

APCI-MS m/z: 409/411 [MH^+].

Example 182

N-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(3-methoxybenzyl)amine bis(trifluoroacetate)

The title compound was prepared from 4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline and 3-methoxybenzaldehyde.

^{1}H NMR (CD_3OD): δ 8.44 (1H, d); 8.11 (1H, d); 7.88 (2H, d); 7.24 (1H, t); 6.97-6.94 (2H, m); 6.83-6.77 (3H, m); 4.43 (2H, s); 3.77 (3H, s).

APCI-MS m/z: 409/411 [MH^+].

Example 183

N-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(2-chlorobenzyl)amine bis(trifluoroacetate)

The title compound was prepared from 4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline and 2-chlorobenzaldehyde.

^{1}H NMR (CD_3OD): δ 8.46 (1H, d); 8.13 (1H, d); 7.90 (2H, d); 7.45-7.40 (2H, m); 7.29-7.25 (2H, m); 6.78 (2H, d); 4.57 (2H, s).

APCI-MS m/z: 413/415 [MH^+].

Example 184

N-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(4-chlorobenzyl)amine bis(trifluoroacetate)

The title compound was prepared from 4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline and 4-chlorobenzaldehyde.

^{1}H NMR (CD_3OD): δ 8.48 (1H, d); 8.14 (1H, d); 7.89 (2H, d); 7.39-7.32 (4H, m); 6.79 (2H, d); 4.45 (2H, s).

APCI-MS m/z: 413/415 [MH^+].

Example 185

N-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(1*H*-pyrazol-3-ylmethyl)amine bis(trifluoroacetate)

The title compound was prepared from 4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline and 1*H*-pyrazole-3-carbaldehyde.

^{1}H NMR (CD_3OD): δ 8.57 (1H, d); 8.22 (1H, d); 7.91 (2H, d); 7.60 (2H, d); 6.89 (2H, d); 6.31 (2H, d); 4.49 (2H, s).

APCI-MS m/z: 369/371 [MH^+].

Example 186

N-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(3-chlorobenzyl)amine bis(trifluoroacetate)

The title compound was prepared from 4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline and 3-chlorobenzaldehyde.

APCI-MS m/z: 413/415 [MH^+].

Example 187

[5-({[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]amino}methyl)-2-furyl]methanol bis(trifluoroacetate)

The title compound was prepared from 4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline and 5-(hydroxymethyl)-2-furaldehyde.

APCI-MS m/z: 399/401 [MH^+].

Example 188

N-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(thien-2-ylmethyl)amine bis(trifluoroacetate)

The title compound was prepared from 4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline and thiophene-2-carbaldehyde.

APCI-MS m/z: 385/387 [MH^+].

Example 189

N-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(2-furylmethyl)amine bis(trifluoroacetate)

The title compound was prepared from 4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline and 2-furaldehyde.

APCI-MS m/z: 369/371 [MH^+].

Example 190

N-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(thien-3-ylmethyl)amine bis(trifluoroacetate)

The title compound was prepared from 4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline and thiophene-3-carbaldehyde.

APCI-MS m/z: 385/387 [MH^+].

Example 191

N-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(4-methyl-1*H*-imidazol-5-yl)methyl]amine bis(trifluoroacetate)

The title compound was prepared from 4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline and 4-methyl-1*H*-imidazole-5-carbaldehyde.

APCI-MS m/z: 383/385 [MH^+].

Example 192

N-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(3-furylmethyl)amine bis(trifluoroacetate)

The title compound was prepared from 4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline and 3-furaldehyde.

APCI-MS m/z: 369/371 [MH^+].

Example 193

N-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(1,3-thiazol-2-ylmethyl)amine bis(trifluoroacetate)

The title compound was prepared from 4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline and 1,3-thiazole-2-carbaldehyde.

APCI-MS m/z: 386/388 [MH^+].

Example 194

N-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(4-bromothien-2-yl)methyl]amine bis(trifluoroacetate)

The title compound was prepared from 4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline and 4-bromothiophene-2-carbaldehyde.

APCI-MS m/z: 463/465/467 [MH^+].

Example 195

N-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(1*H*-imidazol-4-ylmethyl)amine bis(trifluoroacetate)

The title compound was prepared from 4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline and 1*H*-imidazole-5-carbaldehyde.

APCI-MS m/z: 369/371 [MH^+].

Example 196

N-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(2-methyl-1*H*-imidazol-5-yl)methyl]amine bis(trifluoroacetate)

The title compound was prepared from 4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline and 2-methyl-1*H*-imidazole-5-carbaldehyde.

APCI-MS m/z: 383/385 [MH^+].

Example 197

N-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(3,5-dimethylisoxazol-4-yl)methyl]amine bis(trifluoroacetate)

The title compound was prepared from 4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline and 2-methyl-1*H*-imidazole-5-carbaldehyde.

APCI-MS m/z: 398.2/400.1 [MH^+].

Example 198

[5-({[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]amino}methyl)-2-furyl]methyl acetate bis(trifluoroacetate)

The title compound was prepared from 4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline and 2-methyl-1*H*-imidazole-5-carbaldehyde.

APCI-MS m/z: 441/443 [MH^+].

Example 199

N-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(5-pyridin-2-ylthien-2-yl)methyl]amine bis(trifluoroacetate)

The title compound was prepared from 4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline and 2-methyl-1*H*-imidazole-5-carbaldehyde.

APCI-MS m/z: 462/464 [MH^+].

Example 200

N-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(1-methyl-1*H*-benzimidazol-2-yl)methyl]amine bis(trifluoroacetate)

The title compound was prepared from 4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline and 2-methyl-1*H*-imidazole-5-carbaldehyde.

APCI-MS m/z: 433.2/435.2 [MH^+].

Example 201

N-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(2-ethyl-1*H*-imidazol-5-yl)methyl]amine bis(trifluoroacetate)

The title compound was prepared from 4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline and 2-methyl-1*H*-imidazole-5-carbaldehyde.

APCI-MS m/z: 397/399 [MH^+].

Example 202

N-[4-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(1-methyl-1*H*-imidazol-5-yl)methyl]amine bis(trifluoroacetate)

The title compound was prepared from 4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline and 2-methyl-1*H*-imidazole-5-carbaldehyde.

APCI-MS m/z: 383.1/385.1 [MH^+].

Example 203

Methyl 4-({[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]amino}methyl)-1-methyl-1*H*-pyrrole-2-carboxylate bis(trifluoroacetate)

The title compound was prepared from 4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)aniline and 2-methyl-1*H*-imidazole-5-carbaldehyde.

APCI-MS m/z: 440/442 [MH^+].

Example 204

N-Benzyl-5-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)pyridin-2-amine bis(trifluoroacetate)

a) 5-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)pyridin-2-ol

Polyphosphoric acid (3 g) was heated to 140 °C and 2,3-diamino-5-bromopyridine (417 mg, 2.22 mmol) and 6-chloronicotinic acid (525 mg, 3.33 mmol) were added. The reaction mixture was stirred overnight at 140 °C. After cooling, ice was added and the pH adjusted to 7 with a saturated solution of sodium hydrogen carbonate. A precipitate was formed which was filtered off and washed with ethyl acetate to afford the title compound (341 mg, 53%).

^{1}H NMR (DMSO-d_6): δ 8.30 (1H, d); 8.29 (1H, d); 8.20-8.17 (1H, dd); 8.14 (1H, d); 6.50 (1H, d).

APCI-MS m/z: 290.9/292.9 [MH^+].

b) 6-Bromo-2-(6-chloropyridin-3-yl)-3*H*-imidazo[4,5-*b*]pyridine

5-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)pyridin-2-ol (300 mg, 1.03 mmol) was added to phosphorous oxychloride (6 ml) and the mixture was stirred at 110 °C for 4 h. The excess phosphorous oxychloride was evaporated off and the remaining oil was purified by flash chromatography using ethyl acetate/heptane as eluent. The title compound was isolated as a yellow solid (139 mg, 44%).

^{1}H NMR (DMSO-d_6): δ 13.91 (1H, brs); 9.21 (1H, d); 8.60-8.57 (1H, dd); 8.48 (1H, d); 8.37 (1H, brs); 7.78 (1H, d).

APCI-MS m/z: 308.9/310.9 [MH^+].

c) *N*-Benzyl-5-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)pyridin-2-amine bis(trifluoroacetate)

6-Bromo-2-(6-chloropyridin-3-yl)-3*H*-imidazo[4,5-*b*]pyridine (20 mg, 0.07 mmol) was stirred in benzylamine overnight at 120 °C. Purification by HPLC afforded the title compound (20 mg, 51%).

^{1}H NMR (CD_3OD): δ 8.72 (1H, d); 8.44 (1H, d); 8.30-8.28 (1H, dd); 8.15 (1H, d); 7.42-7.35 (3H, m); 7.32-7.28 (1H, m); 6.94 (1H, d); 4.65 (2H, s).

APCI-MS m/z: 380.2/382.2 [MH^+].

Example 205

5-(6-Bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)-*N*-(3-methoxybenzyl)pyridin-2-amine bis(trifluoroacetate)

The title compound was prepared from 6-bromo-2-(6-chloropyridin-3-yl)-3*H*-imidazo[4,5-*b*]pyridine and 3-methoxybenzylamine using the method described in Example 204.

^{1}H NMR (CD_3OD): δ 8.74 (1H, d); 8.41 (1H, d); 8.24-8.22 (1H, dd); 8.12 (1H, d); 7.27 (1H, t); 6.96 (2H, d); 6.85 (2H, d); 4.61 (2H, s); 3.78 (3H, s).

APCI-MS m/z: 410.2/412.2 [MH^+].

Screen

Itk LANCE TRF assay

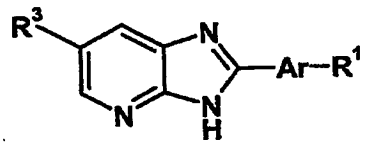
The Itk kinase assay utilized recombinant human Itk kinase domain fused with GST (Glutathione S-Transferase). The protein was expressed in High five insect cells, purified in one step on an affinity chromatography glutathione column and stored in 50 mM Tris/HCl (pH 7.6), 150 mM NaCl, 5% (w/v) mannitol, 1 mM DTT, 30% glycerol at –70 °C. The kinase substrate used in the assay was a biotinylated peptide derived from the Src-optimal substrate (Nair *et al*, J. Med. Chem., 38: 4276, 1995; biotin-AEEEIYGEFEAKKKK).

The assay additions were as follows: Test compounds (or controls; 1 µL in 100% DMSO) were added to black 96-well flat-bottomed plates (Greiner 655076) followed by 20 µL Itk in assay buffer and the reaction was started by adding 20 µL ATP and peptide substrate in assay buffer. The assay buffer constitution during phosphorylation was: 50 mM HEPES (pH 6.8), 10 mM $MgCl_2$, 0.015% Brij 35, 1 mM DTT, 10% glycerol, 160 ng/well Itk, 2 µM peptide substrate and 50 µM ATP. The assay was stopped after 50 minutes (RT) by adding 150 µL ice-cold Stop solution (50 mM Tris/HCl, pH 7.5, 10 mM EDTA, 0.9% NaCl and 0.1% BSA) together with LANCE reagents (2 nM PT66-Eu^{3+}, Wallac AD0069 and 5 µg/mL Streptavidin-APC, Wallac AD0059. Both concentrations were final in stopped assay solution). The plates were measured on a Wallac 1420 Victor 2 instrument with TRF settings after 1h incubation, and the ratio (665 signal/615 signal)*10000 was used to calculate the inhibition values. IC_{50} values were determined using XLfit.

When tested in the above screens, the compounds of Examples 1 to 205 gave IC_{50} values for inhibition of Itk activity of less than 25 µM, indicating that the compounds of the invention are expected to possess useful therapeutic properties.

Claims

1. The use of a compound of formula (I)



(I)

wherein:

R^3 represents halogen, C1 to 3 alkyl or C1 to 3 alkoxy;

Ar represents phenyl, a 5- or 6-membered heteroaromatic ring or an indole ring; said heteroaromatic ring incorporating 1 to 3 heteroatoms independently selected from O, N and S; said phenyl, heteroaromatic or indole ring being optionally further substituted by chloro or OMe;

R^1 represents H, halogen, CN, C1 to 6 alkyl, NO_2, SO_2Me, C1 to 6 alkynyl, CH_2OH, phenyl, OR^2 or $(CH_2)_nNR^4R^5$;

n represents an integer 0 or 1;

R^2 represents H or C1 to 4 alkyl; said C1 to 4 alkyl being optionally further substituted by a group selected from Ar^1, $CONH_2$, CO_2Et, OH, NR^6R^7, halogen and epoxy; and when substituted by NR^6R^7 or halogen, said alkyl is optionally further substituted by OH;

R^4 represents H or C1 to 4 alkyl;

R^5 represents H, C1 to 6 alkyl, C2 to 6 alkanoyl or CH_2Ar^2;

or the group $-NR^4R^5$ together represents a 5 to 7 membered saturated azacyclic ring optionally incorporating one additional heteroatom selected from O, S and NR^8;

R^6 represents H, C1 to 4 alkyl or $CH_2CH_2OCH_3$;

R^7 represents H, C1 to 6 alkyl, C3 to 6 cycloalkyl, Ar^3, a 5 or 6 membered saturated or partially unsaturated heterocyclic ring incorporating 1 or 2 heteroatoms selected independently from O, N and S and optionally substituted by Me, Et or CO_2Et; said C1 to 6 alkyl being optionally substituted by one or more groups selected independently from OH, CN, $CONMe_2$, CONHMe, C1 to 4 alkoxy, halogen, NMe_2, Ar^4, and a 5 or 6 membered saturated heterocyclic ring incorporating 1 or 2 heteroatoms selected independently from O, N and S and optionally also incorporating a carbonyl group; said C3 to 6 cycloalkyl being optionally substituted by OH or CN;

or the group $-NR^6R^7$ together represents a 5 to 7 membered saturated azacyclic ring optionally incorporating 1 additional heteroatom selected from O and NR^9; and optionally substituted by one or more substituents selected independently from OH, NMe_2, $CONH_2$, CH_2OH, CH_2CH_2OH, phenyl, pyridyl, piperidinyl or methoxyphenyl;

R^8 represents H, C1 to 6 alkyl or CH_2Ph;

R^9 represents CH_2CH_2OH, $COCH_3$, Me, CO_2Et, CH_2CH_2OMe or a six membered aromatic or azaaromatic ring optionally further substituted by one or more substituents selected independently from Cl, CN, OMe and CF_3;

Ar^1 represents phenyl, thiazolyl or thiadiazolyl, optionally further substituted by halogen;

Ar^2 represents phenyl, a 5- or 6-membered heteroaromatic ring or a benzimidazole ring; said heteroaromatic ring incorporating 1 to 3 heteroatoms independently selected from O, N and S; said phenyl or heteroaromatic or benzimidazole ring being optionally further substituted by one or two groups independently selected from halogen, C1 to 4 alkyl, CN, CH_2OH, C1 to 4 alkoxy, CO_2Me, CH_2OAc and pyridyl;

Ar^3 represents thiazolyl, triazolyl or tetrazolyl;

Ar^4 represents phenyl, a 5- or 6-membered heteroaromatic ring or an indole ring; said heteroaromatic ring incorporating 1 to 3 heteroatoms independently selected from O, N and S; said phenyl, heteroaromatic or indole ring being optionally further substituted by one or two groups independently selected from halogen and OMe;

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of diseases or conditions in which inhibition of kinase Itk activity is beneficial.

2. The use according to Claim 1 of a compound of formula (I) or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of Th2-driven and/or mast cell-driven and/or basophil driven diseases or conditions.

3. The use according to Claim 2 wherein the disease is asthma.

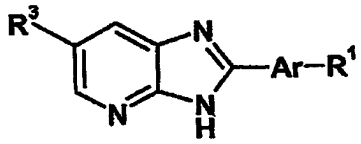
4. The use according to Claim 2 wherein the disease is allergic rhinitis.

5. The use according to any one of Claims 1 to 4 wherein R^3 in formula (I) represents bromo.

6. The use according to any one of Claims 1 to 5 wherein R^1 in formula (I) represents OR^2 or $(CH_2)_nNR^4R^5$.

7. A pharmaceutical formulation comprising a therapeutically effective amount of a compound of formula (I), according to any one of Claims 1, 5 or 6, or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier, for use in the treatment or prophylaxis of diseases or conditions in which inhibition of kinase Itk activity is beneficial.

8. A compound of formula (Ia)



(Ia)

wherein:

R^3 represents halogen, C1 to 3 alkyl or C1 to 3 alkoxy;

Ar represents phenyl, a 5- or 6-membered heteroaromatic ring or an indole ring; said heteroaromatic ring incorporating 1 to 3 heteroatoms independently selected from O, N and S; said phenyl, heteroaromatic or indole ring being optionally further substituted by chloro or OMe;

R^1 represents $(CH_2)_nNR^4R^5$ and n represents an integer 0 or 1;

R^4 represents H or C1 to 4 alkyl;

R^5 represents CH_2Ar^2;

Ar^2 represents phenyl, a 5- or 6-membered heteroaromatic ring or a benzimidazole ring; said heteroaromatic ring incorporating 1 to 3 heteroatoms independently selected from O, N and S; said phenyl, heteroaromatic or benzimidazole ring being optionally further substituted by one or two groups independently selected from halogen, C1 to 4 alkyl, CN, CH_2OH, C1 to 4 alkoxy, CO_2Me, CH_2OAc and pyridyl;

or a pharmaceutically acceptable salt thereof.

9. A compound according to Claim 8 that is:

4-({[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]amino}methyl)benzonitrile

N-benzyl-N-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenyl]amine

N-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenyl]-N-(1H-imidazol-2-ylmethyl)amine

N-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenyl]-N-(1H-imidazol-5-ylmethyl)amine

3-({[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenyl]amino}methyl)benzonitrile

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(4-methoxybenzyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(2-methoxybenzyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(3-methoxybenzyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(2-chlorobenzyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(4-chlorobenzyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(1*H*-pyrazol-3-ylmethyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(3-chlorobenzyl)amine

[5-({[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]amino}methyl)-2-furyl]methanol

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(thien-2-ylmethyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(2-furylmethyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(thien-3-ylmethyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(4-methyl-1*H*-imidazol-5-yl)methyl]amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(3-furylmethyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(1,3-thiazol-2-ylmethyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(4-bromothien-2-yl)methyl]amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-(1*H*-imidazol-4-ylmethyl)amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(2-methyl-1*H*-imidazol-5-yl)methyl]amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(3,5-dimethylisoxazol-4-yl)methyl]amine

[5-({[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]amino}methyl)-2-furyl]methyl acetate

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(5-pyridin-2-ylthien-2-yl)methyl]amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(1-methyl-1*H*-benzimidazol-2-yl)methyl]amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(2-ethyl-1*H*-imidazol-5-yl)methyl]amine

N-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]-*N*-[(1-methyl-1*H*-imidazol-5-yl)methyl]amine

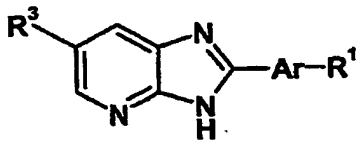
methyl 4-({[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenyl]amino}methyl)-1-methyl-1*H*-pyrrole-2-carboxylate

N-benzyl-5-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)pyridin-2-amine

5-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)-*N*-(3-methoxybenzyl)pyridin-2-amine

or a pharmaceutically acceptable salt thereof.

10. A compound of formula (Ib)



(Ib)

wherein:

R^3 represents halogen, C1 to 3 alkyl or C1 to 3 alkoxy;

Ar represents phenyl, a 5- or 6-membered heteroaromatic ring or an indole ring; said heteroaromatic ring incorporating 1 to 3 heteroatoms independently selected from O, N and S; said phenyl, heteroaromatic or indole ring being optionally further substituted by chloro or OMe;

R^1 represents OR^2;

R^2 represents C3 to 4 alkyl substituted by NR^6R^7 and by OH;

R^6 represents H, C1 to 4 alkyl or $CH_2CH_2OCH_3$;

R^7 represents H, C1 to 6 alkyl, C3 to 6 cycloalkyl, Ar^3, a 5 or 6 membered saturated or partially unsaturated heterocyclic ring incorporating 1 or 2 heteroatoms selected independently from O, N and S and optionally substituted by Me, Et or CO_2Et; said C1 to 6 alkyl being optionally substituted by one or more groups selected independently from OH, CN, $CONMe_2$, CONHMe, C1 to 4 alkoxy, halogen, NMe_2, Ar^4, and a 5 or 6 membered saturated heterocyclic ring incorporating 1 or 2 heteroatoms selected independently from O, N and S and optionally also incorporating a carbonyl group; said C3 to 6 cycloalkyl being optionally substituted by OH or CN;

or the group $-NR^6R^7$ together represents a 5 to 7 membered saturated azacyclic ring optionally incorporating 1 additional heteroatom selected from O and NR^9; and optionally substituted by one or more substituents selected independently from OH, NMe_2, $CONH_2$, CH_2OH, CH_2CH_2OH, phenyl, pyridyl, piperidinyl and methoxyphenyl;

R^9 represents CH_2CH_2OH, $COCH_3$, Me, CO_2Et, CH_2CH_2OMe or a six membered aromatic or azaaromatic ring optionally further substituted by one or more substituents selected independently from Cl, CN, OMe and CF_3;

Ar^3 represents thiazolyl, triazolyl or tetrazolyl;

Ar^4 represents phenyl, a 5- or 6-membered heteroaromatic ring or an indole ring; said heteroaromatic ring incorporating 1 to 3 heteroatoms independently selected from O, N and S; said phenyl, heteroaromatic or indole ring being optionally further substituted by one or two groups independently selected from halogen and OMe;

or a pharmaceutically acceptable salt thereof.

11. A compound according to Claim 10 that is:

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-pyrrolidin-1-ylpropan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-morpholin-4-ylpropan-2-ol

1-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}pyrrolidin-3-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-piperidin-1-ylpropan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-(diethylamino)propan-2-ol

1-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}piperidin-4-ol

1-(4-acetylpiperazin-1-yl)-3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[3-(dimethylamino)pyrrolidin-1-yl]propan-2-ol

4-[({2-hydroxy-3-[4-(6-methyl-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]propyl}amino)methyl]phenol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(2-hydroxyethyl)(methyl)amino]propan-2-ol

3-[{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}(methyl)amino]propanenitrile

4-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}piperazin-1-ol

N^2-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}-N^1,N^1,N^2-trimethylglycinamide

1-[benzyl(methyl)amino]-3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[methyl(2-phenylethyl)amino]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-(4-phenylpiperazin-1-yl)propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-(4-pyridin-2-ylpiperazin-1-yl)propan-2-ol

1-[2-({3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}amino)ethyl]imidazolidin-2-one

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(3-methoxybenzyl)amino]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(2-chlorobenzyl)amino]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(4-chlorobenzyl)amino]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(3-chlorobenzyl)amino]propan-2-ol

ethyl 4-({3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}amino)piperidine-1-carboxylate

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[4-(2-methoxyethyl)piperazin-1-yl]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-(cyclopropylamino)propan-2-ol

3-({3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}amino)propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(2-methoxyethyl)amino]propan-2-ol

2-({3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}amino)propan-1-ol

1-(benzylamino)-3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(pyridin-3-ylmethyl)amino]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(pyridin-4-ylmethyl)amino]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(1-ethylpiperidin-3-yl)amino]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(2-morpholin-4-ylethyl)amino]propan-2-ol

1-[3-({3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}amino)propyl]pyrrolidin-2-one

1-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}piperidin-3-ol

1-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}prolinamide

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[4-(hydroxymethyl)piperidin-1-yl]propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[2-(hydroxymethyl)piperidin-1-yl]propan-2-ol

1-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}piperidine-4-carboxamide

1-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}piperidine-3-carboxamide

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[4-(2-hydroxyethyl)piperazin-1-yl]propan-2-ol

2-(4-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}piperazin-1-yl)benzonitrile

6-(4-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}piperazin-1-yl)nicotinonitrile

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-(1,3-thiazol-2-ylamino)propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-(4-pyrazin-2-ylpiperazin-1-yl)propan-2-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[(2-methoxybenzyl)amino]propan-2-ol

4-[{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}(methyl)amino]cyclohexanecarbonitrile

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-(2-pyridin-3-ylpiperidin-1-yl)propan-2-ol

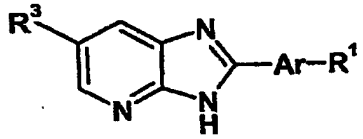
1-{3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}-4-phenylpiperidin-4-ol

2-({3-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-2-hydroxypropyl}amino)-3-methylbutan-1-ol

1-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]-3-[4-(3-methoxyphenyl)piperazin-1-yl]propan-2-ol

or a pharmaceutically acceptable salt thereof.

12. A compound of formula (Ic)



(Ic)

wherein:

R^3 represents halogen, C1 to 3 alkyl or C1 to 3 alkoxy;

Ar represents phenyl, a 5- or 6-membered heteroaromatic ring or an indole ring; said heteroaromatic ring incorporating 1 to 3 heteroatoms independently selected from O, N and S; said phenyl, heteroaromatic or indole ring being optionally further substituted by chloro or OMe;

R^1 represents OR^2;

R^2 represents C2 to 4 alkyl substituted by a group NR^6R^7;

R^6 represents H, C1 to 4 alkyl or $CH_2CH_2OCH_3$;

R^7 represents H, C1 to 6 alkyl, C3 to 6 cycloalkyl, Ar^3, a 5 or 6 membered saturated or partially unsaturated heterocyclic ring incorporating 1 or 2 heteroatoms selected independently from O, N and S and optionally substituted by Me, Et or CO_2Et; said C1 to 6 alkyl being optionally substituted by one or more groups selected independently from OH, CN, $CONMe_2$, CONHMe, C1 to 4 alkoxy, halogen, NMe_2, Ar^4, and a 5 or 6 membered saturated heterocyclic ring incorporating 1 or 2 heteroatoms selected independently from O, N and S and optionally also incorporating a carbonyl group; said C3 to 6 cycloalkyl being optionally substituted by OH or CN;

or the group $-NR^6R^7$ together represents a 5 or 6 membered saturated azacyclic ring optionally incorporating 1 additional heteroatom selected from O and NR^9; and optionally substituted by one or more substituents selected independently from OH, NMe_2, $CONH_2$, CH_2OH, CH_2CH_2OH, phenyl, pyridyl, piperidinyl or methoxyphenyl;

R^9 represents CH_2CH_2OH, $COCH_3$, Me, CO_2Et, CH_2CH_2OMe or a six membered aromatic or azaaromatic ring optionally further substituted by one or more substituents selected independently from Cl, CN, OMe and CF_3;

Ar^3 represents thiazolyl, triazolyl or tetrazolyl;

Ar^4 represents phenyl, a 5- or 6-membered heteroaromatic ring or an indole ring; said heteroaromatic ring incorporating 1 to 3 heteroatoms independently selected from O, N and S; said phenyl, heteroaromatic or indole ring being optionally further substituted by one or two groups independently selected from halogen and OMe;

or a pharmaceutically acceptable salt thereof,

with the provisos that:

i) when R^6 represents H or C1 to 4 alkyl, R^3 does not represent unsubstituted C1 to 4 alkyl; and

ii) that the group $-NR^6R^7$ does not represent unsubstituted morpholine, thiomorpholine, 4-methylpiperazine or 4-phenylpiperazine.

13. A compound according to Claim 12 that is:

6-bromo-2-[4-(2-{4-[3-chloro-5-(trifluoromethyl)pyridin-2-yl]piperazin-1-yl}ethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine

6-bromo-2-[4-(2-piperidin-1-ylethoxy)phenyl]-3*H*-imidazo[4,5-*b*]pyridine

6-bromo-2-[4-(3-piperidin-1-ylpropoxy)phenyl]-3H-imidazo[4,5-b]pyridine

6-bromo-2-[4-(3-pyrrolidin-1-ylpropoxy)phenyl]-3H-imidazo[4,5-b]pyridine

N-{2-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]ethyl}-*N*-(tetrahydrofuran-2-ylmethyl)amine

6-bromo-2-[4-(2-pyrrolidin-1-ylethoxy)phenyl]-3H-imidazo[4,5-b]pyridine

2-[{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}(methyl)amino]ethanol

3-[{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}(methyl)amino]propanenitrile

1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}pyrrolidin-3-ol

1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N,N-dimethylpyrrolidin-3-amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N,1-dimethylpyrrolidin-3-amine

N~2~-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N~1~,N~1~,N~2~-trimethylglycinamide

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-ethyl-N',N'-dimethylethane-1,2-diamine

N-benzyl-N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-methylamine

2-{4-[2-(4-acetylpiperazin-1-yl)ethoxy]phenyl}-6-bromo-3H-imidazo[4,5-b]pyridine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N,N-bis(2-methoxyethyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-methyl-N-(2-phenylethyl)amine

6-bromo-2-{4-[2-(4-pyridin-2-ylpiperazin-1-yl)ethoxy]phenyl}-3H-imidazo[4,5-b]pyridine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-[3-(1H-imidazol-1-yl)propyl]amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(4-methoxybenzyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(3-methoxybenzyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(4-chlorobenzyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(3-chlorobenzyl)amine

ethyl 4-({2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}amino)piperidine-1-carboxylate

6-bromo-2-(4-{2-[4-(2-methoxyethyl)piperazin-1-yl]ethoxy}phenyl)-3H-imidazo[4,5-b]pyridine

1-({2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}amino)propan-2-ol

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(2-methoxyethyl)amine

2-({2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}amino)propan-1-ol

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(2-furylmethyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(tetrahydrofuran-2-ylmethyl)amine

N-benzyl-N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(pyridin-3-ylmethyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(pyridin-4-ylmethyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(thien-2-ylmethyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(1-phenylethyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-1-ethylpiperidin-3-amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(2-morpholin-4-ylethyl)amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-(2-methoxybenzyl)amine

1-[3-({2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}amino)propyl]pyrrolidin-2-one

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-[2-(4-chlorophenyl)ethyl]amine

4-[{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}(methyl)amino]cyclohexanecarbonitrile

1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperidin-3-ol

6-bromo-2-{4-[2-(2-pyridin-3-ylpiperidin-1-yl)ethoxy]phenyl}-3H-imidazo[4,5-b]pyridine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-cyclopentylamine

1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-4-phenylpiperidin-4-ol

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-[2-(1H-imidazol-4-yl)ethyl]amine

1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperidine-3-carboxamide

6-bromo-2-{4-[2-(4-pyrazin-2-ylpiperazin-1-yl)ethoxy]phenyl}-3H-imidazo[4,5-b]pyridine

(1*S*,2*S*)-2-({2-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]ethyl}amino)cyclohexanol

6-bromo-2-(4-{2-[4-(3-methoxyphenyl)piperazin-1-yl]ethoxy}phenyl)-3H-imidazo[4,5-b]pyridine

(1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperidin-4-yl)methanol

4-({2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}amino)cyclohexanol

(1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperidin-2-yl)methanol

1'-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-1,4'-bipiperidine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-1,3-thiazol-2-amine

1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperidine-4-carboxamide

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-1H-1,2,4-triazol-3-amine

2-(4-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperazin-1-yl)benzonitrile

6-(4-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperazin-1-yl)nicotinonitrile

1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}prolinamide

6-bromo-2-(4-{2-[4-(2-methoxyphenyl)piperidin-1-yl]ethoxy}phenyl)-3H-imidazo[4,5-b]pyridine

2-(4-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperazin-1-yl)ethanol

1-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}piperidin-4-ol

6-bromo-2-(4-{2-[4-(2-methoxyphenyl)piperazin-1-yl]ethoxy}phenyl)-3H-imidazo[4,5-b]pyridine

(2*S*)-2-({2-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]ethyl}amino)-3-methylbutan-1-ol

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-4,5-dihydro-1,3-thiazol-2-amine

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-N-[2-(1H-indol-3-yl)ethyl]amine

(2*S*)-2-({2-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]ethyl}amino)-2-phenylethanol

N-{2-[4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenoxy]ethyl}-1H-tetrazol-5-amine

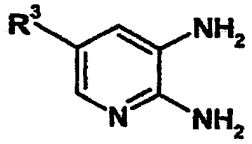
(1*S*,2*R*)-2-({2-[4-(6-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)phenoxy]ethyl}amino)cyclohexanol

or a pharmaceutically acceptable salt thereof.

14. A compound according to any one of Claims 8 to 13, or a pharmaceutically acceptable salt thereof, for use as a medicament.

15. A process for the preparation of a compound of formula (Ia), (Ib) or (Ic) according to any one of Claims 8 to 13 which comprises:

a) reaction of a compound of the general formula (II):



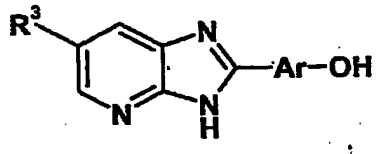
(II)

in which R^3 is as defined in formula (Ia), (Ib) or (Ic),
with a compound of formula (III):

R^1-Ar-CHO (III)

in which R^1 and Ar are as defined in formula (Ia), (Ib) or (Ic), in the presence of an oxidizing agent; or

b) reaction of a compound of formula (IV):



(IV)

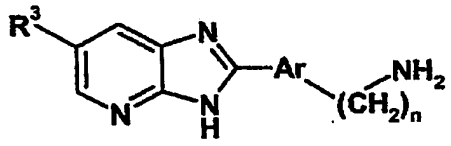
in which R^3 and Ar are as defined in formula (Ib) or (Ic);

with a compound of formula (V):

$$R^2\text{-LG} \qquad (V)$$

in which R^2 is as defined in formula (Ib) or (Ic) and LG represents a leaving group; or

c) reaction of a compound of the general formula (VI):



(VI)

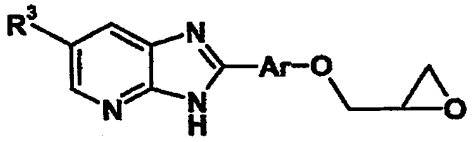
in which n, R^3 and Ar are as defined in formula (Ia);

with a compound of formula (VII):

Ar^2-CHO (VII)

in which Ar^2 is as defined in formula (Ia), or

d) reaction of a compound of the general formula (VIII):



(VIII)

in which R^3 and Ar are as defined in formula (Ib);

with a compound of formula (IX):

HNR^6R^7 (IX)

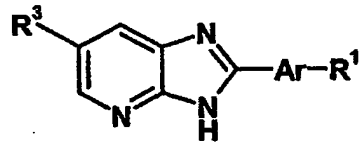
in which R^6 and R^7 are as defined in formula (Ib)

and where desired or necessary converting the resultant compound of formula (Ia), (Ib) or (Ic) or another salt thereof, into a pharmaceutically acceptable salt thereof; or converting one compound of formula (Ia), (Ib) or (Ic) into another compound of formula (Ia), (Ib) or (Ic); and where desired converting the resultant compound of formula (Ia), (Ib) or (Ic) into an optical isomer thereof.

16. A pharmaceutical formulation comprising a therapeutically effective amount of a compound of formula (Ia), (Ib) or (Ic), according to any one of Claims 8 to 13, or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

Abstract

The use of compounds of formula (I)



(I)

wherein R^1, R^3 and Ar are as defined in the Specification and pharmaceutically acceptable salts thereof in the manufacture of a medicament for the treatment or prophylaxis of diseases or conditions in which inhibition of kinase Itk activity is beneficial is disclosed. Certain novel compounds of formula (I), together with processes for their preparation, compositions containing them and their use in therapy are also disclosed.